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**June 1993**  
**No 8**

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# The Physiological Society Magazine

June 1993

## The Physiology Department at University College London



The Physiology department at UCL is 165 years old. After many years of fissiparous activity, our recent history has been of mergers: with the Biophysics department of UCL, with the Physiology department of the Middlesex Hospital Medical School and with the Experimental Pathology department of UCL. Now the

possibility of, and nature of, a future liaison with the Physiology department of the Royal Free Hospital School of Medicine is under discussion.

We currently have 30 HEFC-funded academic staff and a total staff of 130. Six of the academic staff hold joint appointments with departments in the faculty of clinical sciences: Cardiology, Obstetrics & Gynaecology and Nephrology. These appointments are helping to break down the barriers that have sometimes been perceived (or imagined?) here between clinical and basic medical scientists.

### Research

The major research areas can be, rather arbitrarily, classified into: cellular and molecular physiology, neurophysiology, the physiology of cardiac & skeletal muscle, and renal physiology, each of which I have tried to summarise in one of the following paragraphs.

#### a) Cellular and Molecular

Philip Babij investigates the molecular mechanisms regulating growth and development of vascular smooth muscle cells using recombinant DNA and cell biology techniques. David Allan and Paul Quinn work on plasma membrane synthesis and lipid

trafficking. A particular interest is in the processes by which the characteristic lipids of the plasma membrane arrive at their destination from their sites of synthesis in the cell interior.

Bastien Gomperts' group studies exocytotic secretion, the main emphasis being on "regulated" exocytosis, in which cells export materials packaged within membrane-bound vesicles (granules) to the external environment. Peter Tatham works on regulated exocytosis in single cells, and Shamshad Cockcroft on the molecular components that make up the G-protein-regulated phospholipases C and D-mediated transmembrane signalling pathway and their involvement in exocytosis. Anna Koffer studies the role of the cytoskeleton in regulation of the exocytotic process. Does it act as a barrier, preventing vesicles from reaching and fusing with the plasma membrane, or as a transporter of vesicles, using the actomyosin system?

Michael Whitaker's research has centred on how calcium ions act as second messengers because calcium is the crucial regulator at fertilisation in sea urchin and hamster eggs. Second messengers such as calcium, cyclic AMP (cAMP) and the phosphoinositide (PPI) messengers inositol trisphosphate (InsP) and diacylglycerol (DAG) are well known as signal molecules that transmit hormonal signals from the cell membrane to the cell interior. This group is investigating the idea that these second messengers may also be endogenous signal molecules produced by the cell's internal control systems, taking part in cellular regulation in the absence of external signals. Stephen Moss is studying the annexins, a family of ubiquitous  $\text{Ca}^{2+}$ /phospholipid-binding proteins. Interest in these was fuelled by the discovery that two members of the family are the major cellular substrates for phosphorylation by the EGF receptor and  $\text{pp60}^{\text{src}}$  tyrosine kinases.

#### b) Neurophysiology

##### Cellular Neurophysiology

Michael Duchén's studies of mitochondrial function within single mammalian neurones have the objective of identifying interrelationships between changes in mitochondrial function and neuronal activity in single neurones dissociated from the mammalian CNS. Also, in association with Tatham and Gomperts, he studies changes in  $[\text{Ca}^{2+}]$ , and secretion from single cells. Jonathan Fry studies how the inhibitory amino acid neurotransmitters gamma-aminobutyric acid (GABA) and glycine bind at specific receptors in the mammalian central nervous system (CNS). David Attwell and Peter Mobbs work on neuromodulation, the alteration of neuronal properties during normal function and in brain anoxia or ischaemia. Peter Mobbs also investigates the blood brain barrier in the surface capillaries of the neural retina.

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Stephen Bolsover is investigating the role of intracellular calcium in the control of the growing axon. Keith Caddy studies the growth and development of the cerebellum; mutant mice and explants of normal and mutant cerebellar cortex are being studied to look at the interactions between genetically normal and mutant neurones.

Lynn Bindman's laboratory studies long-term potentiation (LTP) and depression (LTD) of synaptic transmission in the rat neocortex and hippocampus. Tony Gardner-Medwin researches memory mechanisms and the disturbances of the neural environment which occur, for example, in ischaemia and the phenomenon of spreading depression, which may occur during migraine attacks.

#### **Whole Animal and Human Neurophysiology**

Brenda Cross and Steve Semple are investigating the way in which the oscillatory component of arterial blood gas composition is used in the control of breathing in health and disease with special reference to exercise. Mark Hanson and Ray Noble are in the Fetal and Neonatal Research Group (based in the department of Obstetrics & Gynaecology - in conjunction with C H Rodeck and J A D Spencer). They are investigating several aspects of foetal physiology but are particularly interested in the integration of physiological systems which occurs during birth and postnatal development.

David Holder studies non-invasive imaging of regional activity in the brain using electrical impedance tomography (impedance imaging). Bruce Lynn works on the neuroimmune interactions in the skin that involve unmyelinated nerve fibres, particularly the nociceptor fibres. Philip Harrison's interests centre around elucidating the spinal mechanisms involved in the control of movement, in particular by investigating the role of interneurons in mediating descending commands from the brain, and in mediating reflexes. John Stephens and Linda Harrison study human motor development in health and disease. They have developed a new electrophysiological technique that allows changes in the pattern of synaptic connectivity that accompanies development to be studied for the first time directly in man.

#### **c) Cardiac and Skeletal Muscle**

Sally Page and Rolf Niedergerke carry out research concerned with the mechanisms by which calcium influx and release from heart cells regulates the strength of the heart beat. Peter Sutton (in conjunction with P I Taggart, Consultant Cardiologist) aims to provide a link between the unexplained association of abnormalities of left ventricular wall motion and sudden cardiac death. Derek Yellon (Hatter Institute for Cardiovascular Studies) leads a rapidly expanding group, which now has more than 20 members, whose principal interest is myocardial protection. More specifically, this Group's interest involves the mechanism of ischaemic preconditioning as well as the involvement of stress proteins in myocardial protection. Roger Woledge's research group measure the energetic costs of contraction in isolated skeletal muscle and muscle fibres. This work is done in collaboration with Nancy Curtin. Also, in collaboration with Stuart Bruce, they are studying the effects of aging on the muscles of mice and humans, finding that oestrogen insufficiency is a major cause of muscle weakness.

#### **d) Renal Physiology**

Robert Unwin joined the Institute of Nephrology at UCL in January 1992 with a joint appointment in the Department of

Physiology, bringing basic research on kidney tubule function into the Department for the first time in many years. Barbara Banks is also involved in an interdisciplinary approach to problems in renal physiology including the absorption of phosphates from the gastrointestinal tract and the nephro-toxic and oto-toxic side effects of amino-glycoside antibiotics.

#### **Teaching**

The teaching commitments of the Department are also quite diverse. We now have an annual quota of 200 medical students, but no longer teach dental students. More recently we have become involved, in collaboration with the relevant schools, in the education of other Health Service professions: four year BSc courses for physiotherapists and for podiatrists (quota about 25 of each) and Project 2000 nursing students (quota 250). With the School of Physiotherapy we offer an MSc in physiotherapy. The long running BSc degree in Physiology continues with about 20 entrants each year, and has now been joined by a joint Physiology/Pharmacology degree with a similar number. In the third year these students are joined by medical students intercalating a BSc, which remains a popular option in spite of the well known difficulties of funding. Physiology is also a commonly chosen course for students doing Chemistry, Medicinal Chemistry, and of course Pharmacology, so our first year science Physiology class has well over a hundred students. We also participate with other Life Science departments in teaching Cell Biology students. In the last few years we have tried with some success to increase the number of PhD students in the Department: we now have 30 and hope for further increases.

Of course, the Physiology department has no monopoly of the study of physiological sciences at UCL. The long established and distinguished Anatomy and Pharmacology departments will be well known to Members for their physiological research and contributions to the Society, usually well represented when the Society visits UCL. A relevant new scientific development at UCL is the opening of the Eisai London Research Laboratory in the new Bernard Katz Building under its director Dr Lee Rubin. Also the new building for the MRC Centre for Molecular Cell Biology (director Professor CR Hopkins) is almost complete. On behalf of all the local physiologists, I extend to The Physiological Society a warm welcome to UCL.

**Roger Woledge**

*See Events section for reports on Leicester Meeting and for details of Designated Sessions to be held at the University College London Meeting.*

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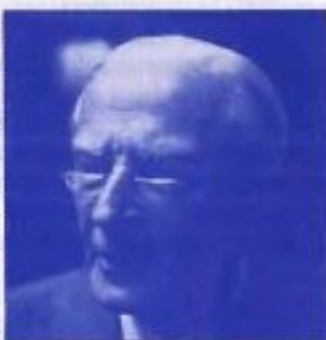
## Memorable experiences in research

Articles in this section were commissioned by Tilli Tansey

In 1953 some of the distinguished guests at the opening of the Charles H Best Institute in Toronto were invited to reflect on the scientific investigations that had given them most pleasure. The President of the Royal Society, E D Adrian, chose to describe one day's experiment in the early 1920s, and the text of his account is here reproduced in its entirety.

### One day's experiment

"It is a very great honour to take part in this presentation. I'm not really very clear what you would like me to do, but I thought it would be best merely to describe one day's experiment which was, to me, an exceedingly enjoyable experience. The pleasure came not so much from doing the work as from realizing suddenly that I had found a way of doing a great deal more. I'm afraid that the argument will be mainly concerned with the techniques of electro-physiology, but it does illustrate the way things go sometimes without the need for any excessive hard work or excessive thought.



It was in the early 20's. I had taken up electro-physiological research on the central nervous system and had spent a great deal of time making string galvanometer records of action currents in the hope of being able to find out exactly what was coming down the nerve fibres when the muscle contracted. We knew then that nerves sent down nerve impulses as signals, but we didn't know anything about the way in which the impulses would follow one another. We didn't know whether they came at a high frequency, or at a steady frequency. We didn't know whether the frequency varied or not. In fact, we didn't know at all how the nervous signals were controlled. Alexander Forbes had been working with me in Cambridge and I had learned a great deal from him about string galvanometers and about mammalian preparations, but the experiments I had started became more and more unprofitable. You know the sort of thing that happens - they became more and more complicated and the evidence more indirect, and after a time it was quite clear that I was getting nowhere at all. But it was fairly clear at that time that the valve amplifier was going to make it very much easier to record action potentials, particularly very small ones, and there had been various descriptions of valve amplifying arrangements. In particular, Gasser and Newcomer had used a three-stage one to record action potentials in the phrenic nerve. I had rigged up a single valve one, but it wasn't much good, so having decided that I was getting nowhere, I wrote to Gasser for the details of the arrangement he was using for the phrenic. He was then beginning his studies with the cathode-ray oscillograph on the action potentials of nerve fibres of different sizes, but he gave me a full description of the amplifier that he and Newcomer had used, and I built one to much the same pattern. I knew very little about it and was rather afraid of all the complications in it. When it was ready, I decided to test it using the capillary electrometer which was in the laboratory, built by Keith Lucas about fifteen years before. I used the capillary electrometer because, although it wasn't as sensitive as the string galvanometer, it had the great

advantage of being more foolproof in that it wasn't so easy to break the string if you overloaded it. The amplifier had to be treated with great respect, as in those days the valves were terribly microphonic. The arrangement I had gave a magnification of about 2000, so I set up a pair of non-polarizable electrodes in a shielded chamber, and put the normal accompaniment of physiological research, the frog's nerve-muscle preparation, on the electrodes, to see whether I could get a steady base line. Well, I was distressed, but not very greatly surprised, to find that the base line wasn't a bit steady. It was oscillating rapidly all the time. As soon as the circuit was open there was this constant rapid oscillation going on and I naturally suspected that I was picking up an artifact from somewhere and that I should have to pull the whole apparatus down and stick it all together again and go on for another month or so, getting no results.

I began re-adjusting the apparatus, and then I found that sometimes the oscillation was there (it was a fine, rapid affair) and sometimes the base line was quite steady. There was a ray of hope, and after trying various arrangements, I found that this little oscillation was only there when the muscle was hanging down quite freely, from the knee joint of the frog's nerve-muscle preparation. If the muscle was supported on a glass plate there was no oscillation at all and the base line was quite steady. The explanation suddenly dawned on me, and that was a time when I was very pleased indeed. A stretched muscle, a muscle hanging under its own weight, ought, if you come to think of it, to be sending sensory impulses up the nerves coming from the muscle spindles, signalling the stretch on the muscle. When you relax the stretched muscle, when you support it, those impulses ought to cease.

I don't think it took more than an hour or so to show that was what the little oscillations were. I was able to make photographic records of them, and within about a week I was nearly certain that many of these oscillations were action potentials coming up sensory fibres in the nerve, and what was more, that many of them came from single nerve fibres and that by some extension of the technique it ought to be possible to find out exactly what was happening in single nerve fibres when the sense organs attached to them were stimulated.

That particular day's work, I think, had all the elements that one could wish for. The new apparatus seemed to be misbehaving very badly indeed, and I suddenly found that it was behaving so well that it was opening up an entire new range of data. I'd been bogged down in a series of very unprofitable experiments and here suddenly was the prospect of getting direct evidence instead of indirect, and direct evidence about all sorts of problems which I had set aside as outside the range of the techniques that one could use. The other point about it was that, as I said, it didn't involve any particular hard work, or any particular intelligence on my part. It was one of those things which sometimes just happens in a laboratory if you stick apparatus together and see what results you get."

Adrian, E D (1954) "Memorable experiences in Research". *Diabetes*, vol 3, no 1: 17-18. Copyright (c) 1954 by American Diabetes Association, Inc; and reprinted with permission.

*Inspired by this reminiscence, we are initiating a series in which present Members of the Society are asked to recall their most memorable research experiences. To begin with, J Z Young, Emeritus Professor of Anatomy at University College London, recalls some of his own significant discoveries.*



### Some moments of discovery

I have been very lucky during my research life to have quite a lot of experiences of new and unexpected phenomena. It is very exciting when you suddenly realise that here in front of you is a physiological action that was not known before. Some of my earliest work was on the autonomic nervous systems of fishes. In the course of this I was



stimulating the sympathetic chain of an angler fish and suddenly realised that the pupil was *constricting*. So I switched to the third nerve and it duly *dilated*. Here is something strange! The fish has the same rather odd set of nerves for its iris but they work in the opposite way to mammals. We still do not know why.

From the beginning of my research I resolved to try to find an animal whose brain and behaviour I could study as completely as possible. At first I thought that the lamprey might be suitable, but in fact the brain proved difficult and the behaviour rather boring. However some early experiments on responses to light were exciting. The ammocoete larva of the lamprey lives buried in the mud and has a well developed pineal eye. I noticed that the larva varied in colour, becoming paler every night - but the rhythm stopped after the pineal eye had been removed. I think that this was the first demonstration of a function for the pineal eye, long before melatonin. I also tried the effect of shining a light on various parts of the body and found that the *tail* is light-sensitive and that the impulses are carried to the head by the lateral line nerve. Imagine my surprise when, after cutting the spinal cord and shining a light on the tail, the head moved! Of course, if you live buried in the mud, it makes sense to have light sensitivity in the tip of the tail - but how odd to use the lateral line organs. Evolutionary adaptation is indeed a strangely powerful process.

In the 1920s and early 1930s we were all very excited by studies of action potentials and synaptic excitation and we kept looking for suitable nerves to work on. I suggested to Jack Eccles that we should look at the giant nerve fibres of earthworms, and we did this in collaboration with Ragnar Granit, who was in Oxford at the time. I did the dissection and Jack the recording, while Ragnar sat in a deck-chair thinking, I suppose. Anyhow, we got fine nerve impulses and they travelled in both directions across the transverse barriers in each segment.

But these earthworm nerve fibres cannot be isolated and cleaned, as can the giant fibres of squids, which I came upon later. I was actually looking for a little organ that we called the epistellar body, which is an orange spot on the stellate ganglion of an octopus. Trying to find it in squids, I could see only some large clear channels, which I took to be veins. Only later did I realise that they are enormous nerve fibres. The proof of their nature had to wait for experiments at Woods Hole in 1936. The proof is easy: you stimulate the nerve close to the ganglion and the mantle muscles give massive contraction; then you prick the giant fibre with a pin and later get little or no response. Actually the situation is more complex, because there are also many small fibres in the nerve. Recording action potentials of the giant fibre was a bit harder at first. I tried, with the help of Detlev Bronk, Ralph Gerard and Keffer Hartline, but all we could get were huge swings on the oscilloscope screen. So one day, when the

big boys were out sailing, Keffer and I hooked up to a loud speaker and put oxalate on the nerve, giving a lovely buzz of single impulses!

The giant fibre system has much more to offer neurology besides its membranes. The axons of the two giant cells in the CNS fuse completely, so that impulses must go to both sides of the mantle to make the jet. I tried to explain to Sherrington that this is the "exception that proves the rule" that nerves don't fuse. He looked up at me and said, "If you say so, Young, it must be true - but I find it difficult to believe".

Looking at the brains of squids and octopuses led me away regretfully from peripheral nerves, to the beautiful higher centres. Hodgkin and Huxley and their successors have given us wonderfully precise information about nerve impulses but we still have little hard evidence of the changes that take place during learning. Octopuses offer a wonderful opportunity to study this, having separate but similar systems for visual and tactile memory. I remember the thrill when I first realised that the two systems have the same organisation. Studies of learning are laborious and don't give quite the thrills of action potentials, but the results can be exciting. Take an octopus and teach it not to attack a crab shown with a white square, then give it an anaesthetic and remove the vertical lobe. As soon as it comes round it comes out to attack (of course you need controls). I remember showing the little excised piece to my wife Raye and saying, "Here is the memory of an octopus". I was wrong, of course, it is only part of the system. That is the value of the octopus memory centres: they show us how to look at a system that is more complex than *Aplysia* but not quite so hard to study as that of a mammal.

There are many other things to be learned from cephalopods. The statocyst works on the same principle as the vestibular system, with angular acceleration receptors in three planes. Different species show variations in shape and volume of the cavities and cupulae, to provide sensitivity appropriate to different speeds of turning. As one examines each new species, one realises its contribution to a whole picture that is gradually emerging and was quite unknown before.

The visual system of course has camera eyes like our own but with many differences. The axons of the rhabdomes project directly on to the orientated dendrites of cells that I think may be edge detectors; but there is no proof yet. Some of them are large cells and could give good records in slices.

A whole new system of extraocular photoreceptors has emerged from the study of the epistellar body mentioned above. In 1929 I thought it was a gland, but 40 years later, with Howard Bern, Alex Mauro and others, we now know that it contains photoreceptors. By study of many species, Richard Young in Hawaii has shown the many functions of these "eyes", which have no lens or other dioptric apparatus. Some serve to control the counterillumination by which squids eliminate their outline as seen from below. Others of these "photosensitive vesicles" are very large in squids that go down to great depths to breed. So we have found a completely new system of receptors, starting from curiosity about a little orange spot.

Then, lately, Ulli Budelmann and I have been looking at strange eye muscles of squids that run from one eye to the other, joined by a tendon across the midline. Contraction of either muscle must pull on both eyes. This action is used for binocular vision when shooting out the tentacles to catch prey. The surprising thing is that sections of the heads of some deep sea squids show



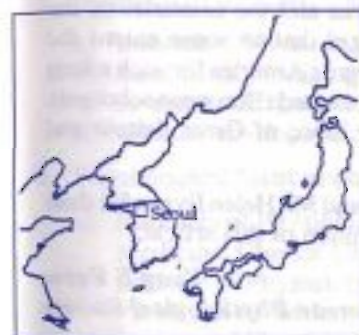
that they also have these muscles and they too must use binocular vision even in the darkness. Perhaps someone will see this from a bathyscope.

With all this I have not neglected the fish guts with which I began. Just this year, Paul Andrews and I have been taking videos of stomach movements of dogfish; some of the movements are retrograde peristalsis. So we were not surprised to find that the dogfish can vomit. Evidently being sick involves some very

ancient mechanism, the discovery of which may help the search for relief of nausea in cancer patients.

The physiology of non-mammalian animals can certainly be of clinical help, but its main value is that it shows us the true nature of living processes, both common factors that run throughout and the variations induced by different environments. Natural selection has presented us with a wonderful series of experiments that we could never have done for ourselves.

*J Z Young*



## Physiology in Korea

### Background

The Korean Physiological Society was established following the liberation of Korea from Japanese rule on 30 November 1945. Much in the same way that Michael Foster had set up The

Physiological Society in 1876 in Britain, the Korean version started off with just a small number of physiologists meeting in Professor Kap Soo Rhee's house. However, the Korean War from 1950 to 1953 reduced the advance of all fields of scientific study, physiology included, to little more than a pile of ashes. Although the study of physiology was just about kept going in medical colleges, the standard of work was fairly basic.

For a very long time, conditions were such that neither among college facilities nor in the completely destroyed physiology laboratories was there even a single oscilloscope which could be used. There was hardly any support from the government nor any move to provide any. After the war, research institutes and college facilities were restored but even this provided only a minimum level for student lectures. In keeping with Korean economic development of the past 20 years, it was from the mid 1970s that investment in university research facilities was undertaken and research, in the modern sense, began. With more medical and natural science colleges being established, the number of students majoring in physiology began to increase and now the Korean Physiological Society can boast about 200 members.

### Organisation and Funding

Physiological research in Korea is mainly centred around the Physiology departments of medical colleges. Naturally, physiological research is also carried out in the Physiology departments or the research units of dental, veterinary, pharmacy and technology colleges and institutes.

Research is being undertaken in nearly all areas of physiology, though this is not a very well known fact on the worldwide physiological scene. Recently, and in keeping with world trends, research is now being actively conducted in the areas of cellular physiology, cardiovascular physiology and neuroscience. At present, basic research is mainly handled in university research centres while the national research institutes place more emphasis on applied research.

Funding is being channelled into these areas and there are two main institutions (funding bodies) which provide financial backing: the first is the KRF (the Korean Research Foundation) and the Basic Medicine Research Council, loosely connected and attached to the Ministry of Education. These institutions largely support basic research but only really finance on a relatively small-scale. The other body of support is the KOSEF (the Korea Science and Engineering Foundation) which is affiliated with the Ministry of Science and Technology and which also supports basic research. It sets great store on applied fields of research (and provides comparatively greater financial support) and it is the technological areas which benefit the most from this funding. Physiology thus receives relatively little funding. There is still practically no support from industry but it is to be hoped that this will increase in the future and expectations ride high on a government plan gradually to increase the budget for Research & Development in science and technology to 5% of GNP.

As non-governmental foundations and charitable organisations only provide financial support on a small scale this really does not go very far in supporting research. For a handful of relatively well established older colleges, hospitals and alumni associations form the main body of funding and provide those colleges with funds; nevertheless, on a national scale they are few and far between.



*Prof Dr Erwin Neher and Prof H K Sung, President of the Korean Physiological Society, at the Annual Meeting on 15-16 October 1992.*





Denis Noble and Prof H K Sung at the dinner of the Spring Symposium on the Ionic Channels and Effect of Taurine, on 21 May 1992.

### Activities

For a number of years the Society's activities have largely been divided between the Spring Meeting and Autumn Meeting. The Spring Meeting takes the form of a seminar or symposium and is centred around a particular theme for one day. The Autumn Meeting is an annual general meeting with oral and poster communications and about 70 papers are presented on various fields. In addition to this, every year one or two eminent scholars are invited for the annual Review Lecture. Recently those invited have included Prof E Neher of Germany, winner of the 1991 Nobel Prize in Physiology or Medicine, Prof D Noble of Great Britain, Prof S Chien, and Prof D Partridge from the United States. Last spring at the Ion Channel symposium, Profs D Noble and R Chapman from Great Britain, N Sperelakis and D Kim of the United States, and A Noma and J Azuma of Japan were invited and conducted a most stimulating discussion. In view of this year's IUPS Congress in Glasgow there will be no Spring Meeting but we plan to invite Prof M Ito who was nominated as IUPS President and Prof J Tanji of Japan for the Annual Review Lecture at the Autumn Meeting.

### Publications

Thanks to the recent economic development, the number of Koreans seeing their papers appear in famous foreign journals is increasing. In addition to this, twice a year the Korean Journal of Physiology is published in English and includes a transcript of the Annual Review Lecture. As yet, however, the papers presented have not always had sufficient appeal for recognition in an international publication. Ten years from now we feel will mark an important turning point by which it will be determined whether or not we can attain the standards of advanced countries.

### Prospects

There are currently more than 30 departments of Physiology in Korea but the newly established ones have not yet managed to meet the requirements necessary for research and mainly concentrate on teaching. Colleges and the government employ many in the area of physiology and if funding continues to be forthcoming at the current rate then the outlook for the future is relatively optimistic. As such an assumption is so closely linked to the national economy, the future for Korean science may be ultimately determined by economic policy. Before the Second World War Korean physiological studies were influenced by Japan; post war the influence came from America, yet from now I feel a balance should be maintained while having the opportunity for mutual exchange between Korea and the countries of the Pacific Rim and Europe. I also feel that to some extent the influence of having always lent towards America for such a long time will be complimented by a look towards European scholastic tradition and attitude, particularly those of Great Britain and Germany.

I would like to thank Prof D Noble and Ms Helen Evans for their kind help and advice in the preparation of this article.

Yung E Earm

Foreign Secretary, The Korean Physiological Society

### Czech and Slovak Physiology

Having been asked by the Editor to write a short survey of physiology in our two countries, I first courteously declined knowing full well what a thankless task this would be. Not perhaps because there would be nothing to write about, but primarily because the situation in our two countries is changing so rapidly that some of the information contained in an essay of this kind will probably be out of date in a few months' time. After having been approached a second time, I capitulated and asked Prof J Koryta to help prepare a text which we hope might be of some interest to readers of *The Physiological Society Magazine*.

#### Some history

One of the first Czech physiologists to attain international fame was Georgius Prochaska (1749-1820) whose main interest was in reflex nervous activity. In 1784 he published a book entitled *De functionibus systematis nervosi commentatio*. A contemporary of his, and a world figure in physiology and morphology, was J E Purkyne Purkinje (1787-1869). Purkinje was an honorary member of several scientific societies, including being a Foreign Member of the Royal Society of London. He made a number of original contributions and many of his discoveries still bear his name. During his professorship in Breslau (Wroclaw) he founded, in 1839, the first institute of physiology in the world. Twelve years later he opened another similar institute at the Charles University in Prague.

In the 20th century, a number of illustrious physiologists deserve at least some mention. Vilém Laufberger (1890-1986), another professor at Charles University, succeeded - while still a medical





student - in converting axotil from its neotenic larval stage to an adult organism by feeding it with dried thyroid gland. His other contributions included the discovery of ferritin and formulation of the idea of the cellular lattice. E Babak (developmental physiology) and Z Sevit (pathophysiology of epilepsy) should be mentioned here at least by name. Seven physiologists from our two countries are (or were) Members of The Physiological Society of Britain, three of whom are permanently resident abroad.

Physiological research in our two countries is mainly carried out in institutes of the Academy of Science and in university departments of physiology:

- 1 Institutes of the Czech Academy of Sciences
  - a) Institute of Physiology, Prague
  - b) Institute of Physiological Regulations, Prague
  - c) Institute of Experimental Medicine, Prague
  - d) Institute of Biophysics, Brno
- 2 Physiological Institutes of Czech Universities
  - a) Institutes of Physiology, First of Second Faculties of Medicine, Charles University (CU), Prague
  - b) Institute of Physiology and Clinical Physiology, Third Faculty of Medicine, CU, Prague
  - c) Institute of Physiology, Medical Faculties, CU, in Plzeň and Hradec, Králové
  - d) Institute of Animal Physiology, Faculty of Science, CU, Prague
  - e) Institute of Physiology, Faculty of Medicine, Masaryk University, Brno
  - f) Institute of Physiology, Faculty of Medicine, Palacký University, Olomouc
- 3 Institutes of Slovak Academy of Sciences
  - a) Institute of Normal and Pathological Physiology, Bratislava
  - b) Institute of Experimental Endocrinology, Bratislava
  - c) Institute of Molecular Physiology and Genetics, Bratislava
  - d) Institute of Neurobiology, Kosice
- 4 Physiological Institutes in Slovak Universities
  - a) Department of Physiology, Faculty of Medicine, Comenius University, Bratislava
  - b) Department of Physiology, Faculty of Medicine, Jesenius University, Martin
  - c) Department of Physiology, Faculty of Medicine, Safarik University, Kosice

Needless to say, this list is far from complete, since physiological research is also carried out in departments of pathophysiology, pharmacology, veterinary laboratories and other research facilities.

The main fields of physiological research covered in our two countries are cellular neurophysiology, neurochemistry, neuroendocrinology, and developmental cardiology, endocrinology, physiology of hearing and of vision, prenatal as well as postnatal development of the nervous system, the adaptation of the mammalian organism to cold (nonshivering thermogenesis, thermoregulatory modification during fever and hibernation), circadian rhythms, excitation-contraction coupling in the heart and spontaneous circulatory oscillations, the mechanism of cell membrane excitability and of muscle

contraction and of the changes in the nervous system due to circulatory damage.

More detailed information on the main research trends of individual institutions may be found in Issue 2 of *Physiological Research* (vol 40, 1991) and in a Special Issue circulated to the participants of the Regional IUPS Meeting in Prague (in July 1991) published in the same journal.

### The changing scene

The system of organisation of physiological research, which had been relatively successful in the past several decades, has had its positive and negative aspects, as has the whole field of science and university education in the country. The Soviet model of building a separate, large organisation for basic research resulted in a divorce between basic research and education, heavily damaging the universities. A positive feature stemmed from the fact that the Academy of Sciences was under less ideological pressure than the universities, so it could be a refuge for many scientists who in the eyes of the Communist Party were judged unsuitable for teaching students.

A brain drain in science, already started in 1938 after Munich, emerged anew in 1948 after the Communist takeover, and broke out in full after the Soviet-led invasion of Czechoslovakia in 1968. About 40 Czech and Slovak are now full professors at university clinics, department heads etc in the West.

After the "Velvet Revolution" in 1989, the position of the Academy became rather ambiguous. Its size had relatively exceeded that of analogous institutions in the western world. Money was scarce and the Academy's elected central administration was unable to respond to the demands of restructuring the institution. Now, under fiscal pressure, the necessary steps, unfortunately long overdue, are being taken. The result of these measures are still not known.

### Funding

At present, the funding for physiological research is derived from three sources. A major part is in the form of a direct contribution from the budget of the Republic. This can be supplemented by an internal, competitive, grant system of the Academy and grants from the Ministry of Health to research teams successful in a competition based on a national and/or international evaluation of their projects. The third source of support is from international grants.

Several journals concerned with physiology are published in both republics, *Physiological Research* (formerly *Physiologia Bohemoslovaca*), *Journal of General Physiology and Biophysics*, *Homeostasis* (formerly *Activitas nervosa superior*), *Endocrinologia experimentalis*, *Cor et vasa* and others.

Before its division into national societies, the Czechoslovak Physiological Society had over 800 members and was part of the Purkyne Medical Society. It regularly organised meetings of the Physiological Society biannually in different universities. It is to be hoped that these contacts will continue to flourish in the future. We are convinced that the splitting of our country into two independent states will not deleteriously affect the hitherto friendly and mutually beneficial relations between our two physiological communities.

P Hník and J Koryta





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*Narishige will be exhibiting at the IUPS Congress, where they can be found at stand no 226 & 228*

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## Physiology at the University of Louvain (Leuven), Belgium

The oldest university in the Low Countries (founded in 1425) was also the first with an officially documented nomination for a chair in the Institution of Medicine with explicit teaching

duties "about physiology and hygiene with related experiments in physics and anatomy...". The date was 1794 and the nominee was P Ch Weber, born in London in 1746. After the troubled times of the French occupation, the university was reopened as a state university in 1817 under the aegis of the United Kingdom of The Netherlands. The Faculty of Medicine's programme included physiology and G-H van Gobbelschroy, the pathology professor of the "ancien régime" university was put in charge. After more troubles and the reopening of the Catholic University of Louvain in 1835, the Faculty of Medicine prospered but no eminent physiologist was in charge until 1912.

A K Noyons, a young Dutch physiologist trained by Zwaardemaker in Utrecht, was then appointed to the chair with instructions to build a new institute of physiology. The official opening took place in 1919 and the impressive building at the Dekenstraat was rightly considered as the best conceived institute of physiology in Europe at that time!

After Prof Noyon's return to Utrecht in 1926, Prof JP Bouckaert took over the chair and, under his stimulating direction, physiology flourished in Leuven in parallel French and Dutch (Flemish) speaking sections.

In the early 1970s, the University of Louvain was split into two geographically separated, independent entities: the Katholieke Universiteit Leuven (KUL), being the Dutch speaking part located in Leuven, and the Université de Louvain (UCL), located in Louvain-la-Neuve and in Woluwe.

The department of physiology of the KUL vacated the old building of the Institute of Physiology at the Dekenstraat in 1976 and is now located in the new medical campus of the Gasthuisberg on the outskirts of Leuven. The department has a staff of five full professors and ten academics plus a number of postdocs, PhD students and visitors (about 15) and a technical staff of 15 members. The department teaches physiology, pathophysiology, and neurophysiology to preclinical medical students, students of dentistry, psychology, education science, and physical education.

The research interests of the department fall into four main groupings. One group, under E E Carmeliet, studies the electrophysiology of excitation-contraction coupling in cardiac cells, using single cell techniques and microfluorometric methods. Another group, led by R Casteels, studies smooth muscle physiology, with particular interest being paid to  $\text{Ca}^{++}$  handling of vascular smooth muscle (using confocal microscopy) and endothelial cell physiology (B Nilius). The third group's interest is in ionic transport in epithelial tissue at the cellular level, the techniques being used including noise analysis and  $\text{Ca}^{++}$  imaging. Finally, one group studies the dynamic properties of visual cortical neurones in cats and monkeys.

The physiology department of the UCL is located less than ten miles from Leuven in Woluwe, a suburb of Brussels. The department consists of 15 academics, a number of temporary positions for PhD and postdoctoral fellows and about ten permanent technicians. The range of teaching duties is similar to that of the department at KUL.

The department at UCL has a tradition of research on skeletal muscle. This was started in 1930 by Prof Bouckaert with Prof A V Hill at University College London. This line of research was pursued by X Aubert, working on calorimetric measurements under A V Hill in the early 1950s, and by G Maréchal who worked in Prof A Huxley's lab in the mid 1960s. Skeletal and smooth muscle energetics,  $\text{Ca}^{++}$  control and differentiation are the research subjects of G Maréchal, J M Gillis and L Lebacqz. H Pouleur and his co-workers study the mechanics of the intact heart and haemodynamics. The electrophysiology and secretion of pancreatic B cells are studied by J Cl Henquin and his co-workers, while Th Godfraind is mainly interested in  $\text{Ca}^{++}$  channels in vascular smooth muscle and their interaction with drugs. The neurophysiologists concentrate their efforts on the study of sensorimotor co-ordination, eye movements and in vitro electrophysiology of LTP in hippocampal slices.

Some funding for research in both departments comes from the annual research budgets from the university (derived from mostly public funds of the national education ministry), but most research funding comes from Medical Research Council grants, National Research Council grants as five year grants to inter-university networks, grants to research groups rated as excellent. European funds account for an increasing proportion of the overall research funds and research agreements with the biotechnology and pharmaceutical industry are supplementing the voracious needs of modern day-to-day research.

*Pierre-Paul Van Bogaert  
(abridged version of article supplied by author)*

### NATO ADVANCED RESEARCH WORKSHOP

#### *Nonlinear phenomena in excitable physiological systems*

to be held at Leeds University from Sunday to Thursday, 8-12 August 1993, (directly after the Glasgow Congress).

This workshop will coordinate recent mathematical and computational results on nonlinear phenomena in excitable media with experimental observations on electrical activity in cardiac muscle, and to consider the effects that the consequences of electrical activity (intracellular  $\text{Ca}$ , mechanical activity) have on the propagative activity that produced them.

This will be principally by reviewing the behaviour of models of excitable cells and tissues and their applicability to cardiac tissue and arrhythmias, but oscillatory and chaotic activity in other, but less intensively studies, excitable physiological systems will also be included.

The Wellcome Trust have provided a grant to enable some UK mathematical biology postgraduates and recent postdocs to attend this meeting; if you are a mathematically inclined physiologist interested in attending, please send a brief CV, your E-mail address and give, in less than 200 words, an explanation of your interest in the workshop to: Dr Arun V Holden, Dept of Physiology, University of Leeds, Leeds LS2 9JT.



# Committee News

## Editor's Note

Readers are asked to note a new feature, instigated following a suggestion by Mary Forsling, which will be appearing in this and subsequent issues of the Magazine: Action Points. This is a bulletin board, which will appear as a boxed item in the Committee News section, giving a quick ready-reference guide to new developments (eg new sources of grants or changes in the regulations) and useful dates (eg imminent deadlines).

## David Cotterrell

David Cotterrell retires as Committee Secretary this year. He was elected to the Committee in 1987, and served as Meetings Secretary for three years from 1988 to 1991 before being elected Committee Secretary. His term of office has coincided with a period of challenge and change for the Society, and throughout he has worked tirelessly in our interests.

Scientific meetings of the Society have changed considerably in recent years: teaching and research symposia are now an important part of every Meeting, and the Designated Sessions of Special Interest Groups have grown to occupy a high proportion of the scientific programme. As Meetings Secretary, David fostered these developments as well as overseeing the introduction of the present system of submission of abstracts on disk and incorporation of editorial changes at the scientific meetings. The Society was fortunate that David had the qualities required of all Meetings Secretaries - they must be well organised, unflappable, discreet and also fairly strong as there is a large and heavy bag to be carried everywhere. The contents of the bag are slightly mysterious, but, as many speakers will know, David has been a reliable source of aspirin on the morning following Society dinners.

David has a profound knowledge of the Society, its idiosyncrasies and its eccentricities, and at the same time is a remarkably efficient and sensitive administrator. This combination of qualities is not common, but it has been fortunate for us, and it explains how as

## Action Points

- ☛ Affiliation: criteria for eligibility redefined, to include physiologists resident overseas - see page 11
- ☛ Grants for the IUPS Congress: the Society will continue to accept grant applications until 21 June - see page 12
- ☛ Southampton Meeting: abstracts may be submitted between 29 June and 9 July
- ☛ Postgraduate Support Fund: applications due in by 31 July - see page 12

Committee Secretary he has been able to guide the Society in ways that have maintained and developed its scientific functions in the unrelentingly harsh environment of the 1990s. An increasing proportion of the detailed work of the Committee is now being done through sub-committees reporting to the main Committee. David has nurtured this system using his characteristic tact and good humour to persuade sub-committees to work on the task in hand, be timely and coherent in their reports, realistic in their expectations and solutions, and to suppress the evolutionary imperative of all committees to self-replicate in perpetuity.

In addition to the domestic work of the Society, David Cotterrell has served as our contact with European physiology and has played a key role in the organisation of FEPS. In this, as in local issues, he has promoted developments and structures that are likely to bear fruit for many years to come. We owe him a considerable debt for his work over the last six years, and wish him well for the future.

Graham Dockray

Members of the Committee at David's last meeting as Committee Secretary, Leicester, April 1993



Left to right, standing: Richard Boyd\*, David Eisner, David Miller, Noel McHale, Cecil Kidd, Denis Noble, Richard Dyball, Gareth Leng, Chris Fry\*, Abe Guz, Peter Ellaway, John Atherton, Kwabena Appenteng, Nick Standen. Seated: Laurence Smaje, Janice Marshall, Jim Gillespie, John Widdicombe, Graham Dockray, David Cotterrell, Ole Petersen, Annetie Dolphin, Richard Vaughan-Jones. (\*) indicates non-members of the Committee asked to be in attendance during the course of the meeting



## Richard Dyball

Richard Dyball is retiring as Press Secretary of the Journal of Physiology, from the Editorial Board, and from the Committee this July. He has been a member of the Editorial Board since 1986, and Press Secretary from 1990. He had previously also served as a Distributing Editor, and has carried a heroic burden of work. Richard has been Press Secretary during interesting times, which have seen the Journal begin the change from traditional production to desktop publishing methods, begin accepting short papers, and consider changes in format. The change in production method has increased the role of the Press Office, which now produces the Journal completely, except for

the final printing. This has involved the appointment of new staff, and a move to larger office space. Richard has been deeply involved in all these changes, and his thoughtfulness and good humour have smoothed their path. He has always been forward looking, while vigorously defending the democratic traditions and interest of the Journal Board and the Press Office. Despite all this Richard has been able to maintain, and indeed extend, his research. I am sure he will welcome the extra time he will now be able to spend on this. Both Board and Society owe him a tremendous amount. We shall miss him and offer him all good wishes for the future.

*Nick Standen*

## Foreign Affiliates - Extension of Affiliation

The Committee has agreed that Affiliation should now be extended so that this form of association with the Society is no longer restricted to physiologists in the UK and Eire. It has also agreed a more detailed definition of the persons eligible for Affiliation, as follows.

This form of association with the Society is intended for physiologists still in the early stages of their careers working in laboratories in the UK, Eire or abroad. It is open to postgraduate students registered for a higher degree in Physiology or a cognate subject and to postdoctoral workers who are not yet Members of the Society. It is expected that postdoctoral workers proposed as Affiliates will normally be (a) within the first five years of attaining a first professional qualification (PhD or medical degree) or (b) awaiting the outcome of their proposal for nomination for election to Membership of the Society.

The fees charged to Foreign Affiliates are calculated to cover fully the run-on printing and postage costs of the literature supplied to them (Notices, Programmes and Magazines, with or without Abstracts, but no Grey Book, Annual Reports or other AGM/SAM material) and are currently as follows: Europe - £30 with Abstracts or £15 without Abstracts; Other Overseas - £35 with Abstracts or £20 without Abstracts. Magazines will be sent by surface mail. The tear-out Affiliation form at the back of this *Magazine* has been amended so that it can be used by any candidate for Affiliation, regardless of residence.

## Affiliates

The Committee extends a warm welcome to the following newly approved Affiliates:

Barry Alexander, Ruth Allchin, Brian Amos, Irina Antonjevic, Lesley Anson, Lachlan Arblaster, Margaret Barnes-Davies, Michael Barry, G David Baxter, A Baydoun, Jane Bird, Joanna Bowtell, John Bradley, Narelle Bramich, Luis-Eduardo Cardona-Sanclemente, Sarah Chen, Beverley Clark, Lynne Clark, Andrew Copestake, Catherine Crichton, Abdullah Demiryurek, Arvinderpal Dhillon, J Doughty, Mark Farrant, Dirk Fledmeyer, Jeni Garbatt, Jonathan Graves, Peter Haddock, Christopher Hillier, Mark Hollywood, Andrea Houghton, Munir Hussain, Seyed Morteza Karimian, Gordon Kennovin, Shihab Khogali,

Wing Hung Ko, Munir Hussain, Sally Jacobs, Ann Jarvis, Sarah Lapper, Vivienne Lee, Jonathan Learmont, Stewart Leitch, Stephen Lynn, Allan MacDonald, Aileen McAinish, James McGarrick, William McKinnon, Linda McLatchie, David Marples, Herve Martin, Caroline Mason, Thomas Matheson, Karen Maubach, J Morris, Hadi Fathi Moghadam, Mostafa Mohammed Naghadeh, Nilda Negretti, James Nichol, Joyce Nicol, Farshad Okhovatsan, Manoj Patel, Monica Pont, Richard Porter, S Przyborski, Neil Reid, Samo Ribaric, Michael Ridding, Justin Rodgers, Sikha Saha, M Sarker, Oona Scott, Jeong Taeg Seo, Peter Skorupski, R Angus Silver, Andrew Southan, Anthony Stanton, Derek Steele, Gary Stephens, Jane St Lambert, Kathy Sutton, Andrew Sykes, Paul Taylor, Andrew Trafford, N Van-Bruggen, Deirdre Walsh, Yun Wang, Andrew Ward, Jane Ward, Ruth Williams, Denham Wisdom, Sharifam Azian Syed Yasin

## Treasurer's Advisory Sub-Committee

(members: John Widdicombe, David Cotterrell, Jim Gillespie, Gareth Leng, Ian McGrath, Nick Standen with Ron Edmondson and Victoria Penrice in attendance)

### *Membership Subscriptions and Affiliate Fees*

The Committee has agreed not to recommend any increase in the rates for Membership subscriptions for 1994, nor in the fees payable by Affiliates for the academic year 1993/94.

### *Personal Accident Insurance*

Due to low take-up, the Society's insurers have been compelled to cut their losses and cancel the personal accident insurance scheme the Society had negotiated at special rates for physiologists.

### *Women Physiologists*

The Treasurer has agreed that Members and Affiliates of the Society be offered a 25% discount for *Women Physiologists*, edited by Lynn Bindman, Alison Brading and Tilly Tansey, and published on the Society's behalf by Portland Press. The book will be on sale at the Congress at its normal price of £9.99 but Members and Affiliates may order their copies now, using the form at the back of this issue of the *Magazine*.



## Journals Management Group

(members: Graham Dockray, David Cotterrell, Richard Dyball, Jim Gillespie, David Jordan, Cecil Kidd, Nick Standen, John Widdicombe)

### *The Journal of Physiology - new format*

The Committee has agreed to give its approval in principle for a move to American A4, double column, soft cover for *The Journal of Physiology*. Designs have been commissioned for a new style of cover and for the internal layout. There will be an opportunity to hear a report on progress at the AGM. However, it has been essential to reach early agreement to take full advantage of the Glasgow Congress to publicise the change. The views of all Members of the Society have been sought by circulation of a fly-sheet.

The transition to in-house preparation of camera ready copy at the Press Office is taking place with impressive efficiency and speed - it is anticipated that practically all material will be dealt with direct from authors' disks by this autumn: this is planned to take effect from the first 1994 volume.

### *Reduction of publication delay*

As Members will notice from the figures given in the Annual Report (and, perhaps, from their own experience), the publication delay for papers appearing in the *Journal* had been creeping up during the past couple of years. This was largely due to maintaining acceptance rates following an increase in submissions after abolition of alphabetical ordering of authors' names. Readers may be pleased to learn that, by taking a variety of steps, the Secretary of the Editorial Board expects the publication delay to be substantially reduced by the end of the year.

### *Abstracts and Proceedings*

The change of *Journal* format has implications for the publication of Abstracts. Much work has been done to explore what effect a change of format would have upon the possible length of Abstracts and published Proceedings, including experiments with draft layouts and consultations with key groups, including Special Interest Group organisers and samples drawn from both the membership and Affiliates. After lengthy discussion, the Committee agreed that the length of abstracts would not be increased. These arrangements will be for a period of one year whilst further discussions on the future of the Proceedings take place.

### *Press Office - New Copy-Editor*

Alison James has joined the Press Office staff as an additional Proof Reader/Copy Editor. Alison has had over four years' experience as a laboratory technician in the experimental classrooms at the Physiological Laboratory, Cambridge University, where, amongst other things, she was involved in the make-up and production of final year undergraduate students' projects. She trained as a copy editor in 1992 at Book House Training Centre, London and has experience of proof reading with the IUPS.

## Education & Information Sub-Committee

(members: John Atherton, Kwabena Appenteng, Geraldine Clough, Simon Howell, Janice Marshall, John Patterson)

### *Cell to Man - Physiology: Education & Career*

By the time this *Magazine* reaches Members, the Society's new careers booklet will be available. Copies are being sent in bulk to major departments and copies will be available at the Society's stand at the Glasgow Congress. Additional copies are available from the Society's Administration Office: please let the staff there know in advance if you would like copies in bulk for your next Open Day or local careers fair or if you are giving a *Talking Point* lecture.

Plans are afoot to prepare a new display stand to stimulate interest in Physiology, which may be borrowed from the Administration Office for use at open days, careers fairs, science festivals etc; and the design of two new posters to promote Physiology has been commissioned. Watch this space for further details.

## Grants Sub-Committee

(members: Graham Dockray, Annette Dolphin, Chris Fry)

### *Postgraduate Support Fund*

Members are reminded that applications for assistance from this Fund should normally be submitted by 31 July. Up to £1,000 may be granted to graduates in Physiology, or a cognate science, engaged in research in the UK in a department of Physiology, or a cognate science, when their supervisor is a Member of the Society. The purpose of the Fund is to provide support for postgraduates in exceptional circumstances, such as periods of ill health, absence of essential facilities, disruption of supervision etc, to assist in the completion of their research projects, and to bridge the period between graduation and the availability of full-time posts for especially gifted students.

### *Financial Difficulties in attending the Glasgow Congress?*

Up to three grants of \$333 (roughly £200) will be made available by the IUPS to support young physiologists (under 35) from the British Isles who would otherwise have difficulty in attending the Congress. Applicants should have already registered for the Congress and should send a letter stating the reason for their difficulty to the Administrator (Grants), The Physiological Society, Administration Office, Oxford OX1 3XE, fax (0865) 798092, by Monday 21 June.

A proportion of the allocation set aside by The Physiological Society to provide grants for physiologists wishing to attend the Congress has not yet been spent. Anyone satisfying the criteria who has not yet applied for a grant is encouraged to do so as soon as possible: the Grants Sub-Committee will continue to review applications until 21 June, or when their funds have been exhausted, if sooner. Full details of the criteria for eligibility appear on the application form, which can be found in the September, December and January issues of the *Magazine* or obtained from your department or from the Administration Office.



## Historical Studies & Archives Sub-Committee

(members: David Whitteridge, Reg Chapman, David Cotterrell, Martin Rosenberg, Julia Sheppard, Tili Tansey)

### *History of The Physiological Society during its First Fifty Years 1876-1926*

This volume, written in 1926 by one of the Society's Founder Members, Sir Edward Sharpey-Schafer, records the first 50 years of the Society's activities. It includes summaries of many of the scientific meetings from that period and brief biographies of Society Members. First published in 1927 as a supplement to *The Journal of Physiology*, copies have been unavailable for many years. The Physiological Society has recently taken the opportunity of reprinting a facsimile of the original, which will make this important account more accessible to those interested in physiology and its history.

Copies of the facsimile edition will be on sale at the IUPS Congress (price: £6). Copies can also be ordered direct from the Society's Administration & Publications Office.

## Clinical Scientists in the Health Service

The Committee has established a small working group, chaired by Abe Guz, to discuss the difficulties of clinical physiologists, such as NHS workers in physiological measurement and what role the Society might play in representing their scientific and professional interests.

## Congratulations

- to Horace Barlow, Peter Bishop and Vernon Mountcastle, on being awarded the Australia Prize for 1993 for their contributions to the understanding of the workings of the brain and the senses of sight and touch. The Australia Prize was first awarded by the Commonwealth Government in 1990 and acknowledges excellence by scientists and technologists in applying their skills for the benefit of humanity. The field which had been selected for the 1993 Prize was sensory perception.

- to Denis Noble on being awarded the Baly Medal for 1993. This award is made in alternate years by the Royal College of Physicians to "the person deemed to have most distinguished himself in the science of physiology, especially during the previous two years". The previous two medal winners were C D Marsden (1991) and M J Berridge (1989).

- to Trevor Lamb on his election as a Fellow of the Royal Society, in recognition of his work on the mechanisms of vision in vertebrate animals, in particular the way the individual receptor cells in the eye respond to light, and his experimental skills in determining the role of certain chemicals in the reception and detection of light and the way the process can be disrupted or distorted.

- to Edward Reynolds on his election as a Fellow of the Royal Society, in recognition of his contributions to scientific methods for overcoming the problems of premature and ill newborn babies, in particular respiratory illnesses, and his use of ultrasound

imaging, magnetic resonance spectroscopy and near-infrared spectroscopy to explain the mechanisms and chances of recovery from brain injury occurring around the time of birth.

- to Sir John Vane on being awarded the Bayliss Starling Prize, the lecture for which is to be given at the Cambridge Meeting in July 1994

- to Annette Dolphin on being awarded the G L Brown Prize for 1993/94

## The Benevolent Fund

The title "Benevolent Fund" has a somewhat archaic ring about it, conjuring up a vision of the charitable acts of the Victorian gentry. This, of course, is not the function of The Physiological Society's Ben Fund (as it is known to all who have had something to do with it). We're stuck with the title though, which was registered with the Charity Commissioners when the Fund was established in 1976.

So what does the Fund do and why was it established? Most Members of The Physiological Society progress through life without major hitches, but there are occasional instances when something goes badly wrong, either for a Member or for their dependants. Since The Physiological Society's charitable objects did not permit it to help its Members directly in such cases, a separate fund was established which, although administered by The Physiological Society and its Members, is formally separate. It can offer a wide range of types of assistance, and each case is considered by the Trustees on its merits.

The Ben Fund has in the recent past mostly been used to help the dependants of Physiological Society Members who die unexpectedly. Death is certainly not the only criterion for assistance, though; the Trustees could help with expenses resulting from illness or unemployment, for instance. In some years there are several calls on the Ben Fund; in others none. The Fund currently has assets of around £21,000 after a couple of quiet years.

The Ben Fund mainly relies on donations from Members. These are most useful in the form of a covenant, which allows the Fund to recover a substantial extra amount in tax. Full instructions on making a covenant are given in the Grey Book. Money has also been raised with the aid of Ben Fund badges ("I'm a benevolent physiologist") and from raffles at Scientific Meeting Dinners. As well as raising money, raffles also have a valuable PR function.

While the money in the Ben Fund is not large, the Trustees are able to react rapidly to a call for help. Often we are dependent on Members alerting us to cases of difficulty; all you need to do is contact one of the Trustees or one of the Officers of The Physiological Society. The current Trustees are:

Mary Forsling, Dept of Obstetrics & Gynaecology, UMDS, St Thomas' Campus, London, tel (071) 928 9292 Ext 2562

Peter McNaughton, Dept of Physiology, King's College London, Strand, London WC2R 2LS, tel (071) 873 2473

Michael de Burgh Daly, Dept of Physiology, Royal Free Hospital School of Medicine, Rowland Hill Street, London NW3 2PF, tel (071) 794 0500

Mike Spyer, Address as Michael de Burgh Daly, tel (071) 431 0009

Peter McNaughton



## Letters and Reports

### Out to Grass

Dear Sir,

You asked me (as a retiring Committee member) to write a piece for the *Magazine* about my views on the directions in which the Society should evolve. My initial reaction was to produce something witty, perhaps along the lines of ten hopes and fears for the future. Fear number one, of course, being that the *Magazine* will eventually be thicker than *The Journal of Physiology*.

On a more serious note, there is one major argument to which the Society can make a significant contribution. The importance of this was brought home by a breakfast time conversation with our 13 year old daughter. She asked casually, through a mouthful of cereal, if she could go for a walk with a friend. This seemed too good to be true - the children are more likely to be found topping up their daily X-ray dose in front of the television rather than out walking. Better still it was going to be a sponsored walk for charity. The only problem was that the "charity" in question was an antivivisection organisation. At this stage her parents immediately lost their usual woolly liberal views.

This example is just one of many which will be familiar to anyone with teenage children. At school they are exposed to a constant barrage of propaganda from antivivisection organisations. Many teenagers are (rightly in my opinion) concerned about the quality of the environment. This is exploited by the antivivisectionists who peddle the false premise that a concern about global warming and pollution requires that one also object to animal experiments. It is obvious that the antivivisectionist arguments, if successful, would bring an end to physiological research. In addition, however, they also serve to turn schoolchildren off science in general. Scientists are portrayed as having provided the atom bomb, pollution and, now, suffering to animals.

There are other organisations, such as the Research Defence Society, which play an important role in countering these arguments. However, The Physiological Society should seize every opportunity to join in. To put the argument at its most crude level: providing the next generation of physiologists requires defending our corner in the classroom.

David Eisner

(Articles on this theme will appear in the next issue of the *Magazine*)

### Society Meetings

Dear Sir,

In the January issue of the *Magazine* (No 6), the Meetings Secretary raised the question of falling standards in the scientific content of Communications at Scientific Meetings. This problem was amply demonstrated at the recent Leicester Meeting of the Society. While the majority of abstracts were of high standard, a number were mainly descriptive and contained little or no hard scientific data. One communication in particular was merely a proposal for experiments that had not yet been performed, utilising equipment that had been neither built nor tested and which required the development of novel fluorescent probes that have yet to be synthesised. This abstract will now be published in the Proceedings in the *Journal* since no Member present during the Communication seemed to feel that it was unworthy of publication. If this is the case, then any Member could submit an abstract detailing experiments that they intend to perform over the next six to twelve months.

Part of the problem appears to be that there are no firm requirements for the submission of abstracts other than those regarding space and formatting. If the standard of abstracts is to be raised then specific minimum requirements should be set. These should include the requirement that abstracts contain numerical data backing any observations or conclusions. Setting such guidelines would allow specific objections to be raised concerning the content of unsuitable or sub-standard abstracts.

The standard of published abstracts should be a matter of concern for every Member (and Affiliate) of the Society, since they represent, to some degree, a view of what the Society considers to be acceptable science.

Hugh Pearson

Dear Sir,

The Meetings Secretary, Dr J I Gillespie, asked for the views of Members about the planning of future Meetings. I would like to express a strong and I believe a fairly common view among Ordinary Members. That is, that the practice of holding mixed Meetings on a variety of topics, as has been done throughout most of the history of the Society, should continue. Any Member should be entitled to give a paper even if that Member believes that it might be unpopular and might be turned down for publication. Any sort of selection of papers to be presented must represent a kind of censorship by the Establishment of the Society, however fair those who selected the presentations attempt to be. I have been perfectly aware that when I have presented papers, for example, questioning the existence in life of the endoplasmic reticulum, or the chemical basis of transmission, or the existence of synapses, many Members would not like these views. However, I believe that many of them accept that I have put forward a reasonable case in good will. Such a situation in which sincere research workers can question in public the generally accepted views of physiologists is healthy because it is one of the important ways by which science progresses. Any procedural change which blocks a Member will be to the detriment of physiology. I would also like to add my personal opposition to the practice of voting after an abstract has been given, on whether it is to be published. It makes assumptions that, firstly, physiologists will react rationally to challenges of deeply held views; secondly, that an audience can assess the validity and implications of novel views in ten minutes; and thirdly, that the validity of a finding is measured both by the number of people who agree with it and by the larger number who did not vote.

Harold Hillman



## Tom Sears to retire

Dear Sir,

It may come as a surprise to many to learn that Tom Sears will soon be retiring from the Sobell Chair of Neurophysiology at the Institute of Neurology at Queen Square. Although he has been actively publishing since the late 1950s and has been a Member of the Society since 1964, he has continued to make such fresh and original contributions to Neuroscience that it is difficult to appreciate that he is about to leave his laboratory.



Tom's career really took off when he went to work for his PhD in Sir John Eccles's lab in Canberra. On his return from there to Queen Square he presented data from intracellular recording from intercostal motoneurons, which, though depending on the techniques learned in Canberra, bore his own clear original mark. He introduced the term "central respiratory drive potentials" for the rhythmically fluctuating depolarisations and hyperpolarisations seen, and published a series of studies exploiting this approach to demonstrate the integration at the motoneuron level of central drive and peripheral feedback, which have served as models for others working on different systems. What was so novel about this was his quantitative emphasis on the summation of barrages of natural, asynchronous inputs, rather than the classical approach of excitation by electrically evoked synchronous volleys.

Innovative methods have always been to the fore in his work, exploiting the most appropriate preparation for his current scientific purpose (those one-technique handle turners amongst us could take notice). With David Stagg, an engineering graduate student, he was among the first to make really effective use of linear systems and signal analysis methods in Neurophysiology. He was soon well-equipped with averagers, multichannel tape recorders and hybrid computing kit and so was well placed to recognise quickly the potential of the spike-triggered averaging (STA) method introduced by Lorne Mendell and Elwood Henneman. So, with Peter Kirkwood, he cut through the confusion surrounding the central projection of muscle spindle secondary afferents and directly demonstrated their monosynaptic input to the motoneurons. The STA method was further extended to measure selectively the conduction velocity of axons over short distances ("pre-trigger averaging"), now widely used for all sorts of purposes. Such cross-correlation methods were given more ingenious twists by the group at Queen Square with the description of "averaged common excitation" (ACE) potentials and, very importantly, the cross correlation of motoneuron firing to reveal shared connectivity. Unfortunately, in a small space one cannot do justice to the full implications of this work, but nearly 20 years on it is still providing the secure basis for elegant studies on connectivity in animals and in man, which could not be done in any other way.

Perhaps for one so skilled in animal experiments it is surprising to find what imaginative work Tom has done in human neurophysiology. I was privileged to join in some of his studies together with John Newsom-Davies on human respiratory muscles at one time. My chief task was to place EMG needles

in intercostals and diaphragm (oh, blessed days before ethical committees!). I do not think it was the pneumothorax which limited our further collaboration, because we have remained on good terms. In fact, it has been one of the pleasures and assets of working in London to be able to go for a chat with him and to come away much wiser, especially regarding the literature, of which he has an unrivalled grasp. Much of Tom's work has been on the respiratory system and he is still working in that field on ideas relating to sudden infant death syndrome. The respiratory system has its own inherent interest, but in a number of cases it has additionally been a convenient general motor control model with the useful property of continuous rhythmic activity. This has been the basis for some important experiments on development and plasticity of spinal connections following injury.

The other area in which Tom's work has probably made most impact is in the mechanism of conduction block in demyelination. He quickly mastered the biophysics of this subject and, with M Rasminsky and H Bostock studied the effects of controlled lesions with diphtheria toxin. The resulting papers were beautifully illuminating and greatly advanced the subject. There is no room to do more than just to list his other important areas of interest, such as the mechanics of the rib cage, respiratory centre mechanisms and interneurons, the cerebellum, analysis of propagation into motor nerve terminals and motoneurons in tissue culture. In all these studies he has attracted colleagues from many countries, through whom his influence will have been widely spread, with untold benefit to our science. Certainly he has been very successful in his international collaborations and with his wife Blanche has made many firm friends around the world, not least through his Presidency of the European Neuroscience Association.

Tom Sears has been a worthy first holder of the Sobell Chair of Neurophysiology and will be a very difficult act to follow.

Tony Taylor

(See Notices section for details of the symposium to honour the career of Tom Sears.)

## Physiology and the Media

Dear Sir,

I cannot be alone in having found your multi-authored feature on Physiology and the Media both hugely instructive and entertaining. But I think that the late Peter Medawar was, for once, mistaken in referring to structured scientific papers as frauds, as reported by Geoff Watts. Of course, the drunkard's walk from idea to experiment to mistake to screams etc is more descriptive of the scientific method than would be gleaned from the form Method:Results:Discussion. But the latter is a report. This allegedly fraudulent system distils clarity from mess, and message from noise. If the reader is familiar with a method, he may glance at its description, but concentrate on the results and, perhaps, the discussion. Alternatively, he may delve into the method, decide that neither the author nor the referees know much about the subject, and not bother about the rest. With *The Journal of Physiology* growing faster than our working lives, the fraud saves time.

Robert Weale



## Elections at the 1993 AGM

### Statements from prospective Committee Members:

As announced in the last issue of the Magazine, all Members standing for election as new members of the Committee were asked to provide a short article containing biographical and bibliographical details and some mention of their contribution to the Society's activities. The replies received are set out below. This is followed by a table of the location, research interests and Sub-Committee duties of the current Committee members eligible for re-election.

### Standing as Ordinary members of the Committee (contested)

Joan Abbott

I began my association with The Physiological Society while working with Hugh Davson at University College, and became a Member in 1975. The research interests of my group at King's College are in the blood-brain barrier and neurone-glia interactions, both relevant to control and signalling within the nervous system. We have developed a number of collaborations, currently with the Marine Biological Association (MBA) Laboratory, Plymouth, and Denmark, Hungary and Japan. We regularly present our work at Physiological Society Meetings, and have published in *The Journal of Physiology*. Two international symposia which I organised (one for the MBA/Physiological Society) have resulted in published volumes (*Glial-Neuronal Interaction*, New York Academy of Sciences 633, 1991; *Cephalopod Neurobiology*, OUP, 1993). I have been a member of the MBA Council, and the Science and Engineering Research Council's Biological Sciences Committee, and I am currently on the editorial boards of *Glia* and *Cerebrovascular and Brain Metabolism Reviews*. At King's I run an MSc course in Biomedical Research, and have been delighted to see how a series of rigorous techniques workshops and a research project can help students develop a real love and aptitude for research.

At its best, The Physiological Society encourages rigorous science, lively debate, technical innovation and educational excellence. Many of us have strong affection and respect for the Society and its traditions, but believe in the need for a balance of tradition and innovation to take into account the needs of the modern scientific community. I am greatly in favour of the recent changes to encourage more participation by younger Members, and to make Meetings more focused by means of Designated Sessions and specialist symposia. We need to do more to forge strong links with European societies, by joint meetings, and by inviting speakers to our symposia. The popularity of special lectures at Meetings shows we have not lost the ability to be interested in subjects outside our own fields, and I believe The Physiological Society can do a great deal to sustain our general education.

I was happy to accept the invitation to stand for the Committee and, if elected, would work hard to maintain the standard and interest of Scientific Meetings and symposia. I would take seriously the need to promote the cause of young scientists, by encouraging their participation in Meetings, and by pressing for a proper career structure in research. As science becomes more complex in its techniques, so that research groupings and "centres of excellence" have operational advantages, we should

surely consider introducing a career structure for research officers to supervise and manage these groups within our universities.

Roger Green

I came to Physiology after medical school principally to study for Primary FRCS. In those far off days it was still possible to act as a demonstrator in Physiology. However, I was attracted by the science and stayed initially for what was supposed to be a short period but has extended to a lifetime! After being elected to the Society in 1971, I spent two years in Gerhard Giebisch's laboratory in Yale where I learnt the art of renal micropuncture. I have been in renal physiology ever since. Shortly after my return, I set up with Dr F Nashat a Renal Group meeting which, after one to two Physiological Society Meetings a year, had a get together with a specialist speaker. This was the forerunner of the Special Interest Groups although then we never met during a Meeting - only after.

In 1978, I was elected to the Editorial Board of *The Journal of Physiology* and for the next seven years was either Distributing Editor or the deputy. In those days there was a single Distributing Editor with a large work load. Latterly I have joined the Editorial Board for *Experimental Physiology* and the Board for Monographs so I still have an interest in the Society's publications.

In 1990, I became Head of Department of a combined Physiological Sciences department at Manchester and have therefore had experience of a wide variety of personnel and physiological problems. I have also become more active in the opposition to the antivivisectionists and have helped in the formation of the Research Health for Charities Group.

Outside the Society, I have recently been on the International Programme Committee for IUPS in Glasgow and a member of their Renal Commission. I also act as Chairman of the European Board of *Physiological Reviews*.

Brian Harvey

I am 36 years of age and have been a Foreign Member of the Society since 1987 and have regularly contributed to Meetings and to *The Journal of Physiology* since 1981. I have spent the past 11 years in France, latterly as a director of research with the Centre Nationale de la Recherche Scientifique (CNRS); was appointed in January 1993 to the Associate Chair of Physiology at the University College, Cork (UCC) and am now an Ordinary Member of the Society. My research interests are epithelial ion and water transport and intracellular signalling. During my years in France I built up a strong international collaboration network and am currently the Evans Visiting Professor at the Department of Physiology, Otago University, New Zealand and Visiting Professor at the August Krogh Institute, Copenhagen. My research position with the CNRS is maintained under a "detachment" agreement with UCC until 1998. To promote my research area in physiology, I have accepted the IUPS invitation to organise the *Epithelia Cross-talk Symposium* in Glasgow and have recently established a new Cellular Physiology Research Unit (CPRU) at UCC. The major challenges facing me on returning to Ireland are the provision of postgraduate training in areas of physiology which Irish graduates have had to seek abroad and the establishment of long term postdoctoral career opportunities. The complete absence of such structures poses a serious threat to the future of Physiology in my country. The setting-up of the CPRU at UCC goes some way in meeting these



challenges; however, for a sustained effort we need encouragement and collaboration from our UK and other European partners.

I gladly accept the invitation to stand for election as an Ordinary member of the Committee and, if elected, would hope to involve The Physiological Society more than ever in the Republic of Ireland and, using my French experience, also in continental Europe. In practical terms, although I have been back in Ireland for only three months, I am actively fostering links between the UK and Eire by offering postgraduate training grants to British physiologists and encouraging their participation in symposia on *Ion Transport in Health and Disease* planned for June 1993 and September 1995 in UCC. The Department of Physiology at UCC will also host a Scientific Meeting of the Society in 1995 to celebrate the 150<sup>th</sup> anniversary of the foundation of the Queen's Colleges in Ireland.

Some of my other objectives include increasing public awareness of basic research, which is being undermined by EC and Government policy-led technology "research". I am convinced that we are engaged in a "dialogue of the deaf" while directly lobbying politicians and their advisors and the way to change is to convince the electorate that our research is important for the long-term health and economy of these islands. Ideas put forward in recent articles in this *Magazine* on dealing with the media could be developed by the Society to help create favourable public exposure.

I would also wish to offer my experience in Europe and with the CNRS to help younger physiologists pursue opportunities in post-Maastricht Europe.

#### *Stephen McMahon*

I am a neuroscientist working in the Department of Physiology at UMDS, London. I am 38 years old. My interest in the somatosensory system spans from the molecular biology of neurotrophins to the psychophysical study of itch.

The need for these biographical statements reflects a growing specialisation and fragmentation of the physiological community. There is an attendant need for The Physiological Society to respond to these changes. I believe this is particularly true in the case of the *Journal*, which, by the nature of the specialised and wide-ranging material it carries, threatens to lose its general appeal.

#### *Brian Whipp*

Physiology is, in many ways, a special science: not least because of its range of perspective. This extends from the precision of atomic nuclei exposed to a magnetic field to the integrated systemic response of an entire organism exposed to environmental stressors. It is important that major unresolved issues in the control of systemic functioning be addressed at the molecular level; it is equally important, however, that the exciting advances in molecular and cellular physiology are considered within the larger framework of systemic physiology.

If elected to the Committee, I would consider it important to ensure that this range of perspective be maintained and fostered within the Society. This is crucial if the tendency towards progressive fragmentation of physiology into isolated levels of organisation is to be countered. Quine's dictum that "Boundaries need not be barriers" seems appropriate in this regard. I would, for example, encourage the presentation of "integrative"

symposia within Meetings of the Society, designed expressly to develop greater interaction and dialogue between physiologists working at different levels of physiological organisation. Such gatherings would also provide a valuable focus for introducing students and young scientists to the range of opportunities physiology has to offer in and beyond the 1990s. While naturally supporting excellence in research at all levels of physiological organisation, I would encourage innovation in the teaching of physiology, exploiting the opportunities of new technology.

I also believe it important to attract greater numbers of clinically trained scientists into physiology and hence into the Society. Having for 20 years held a joint appointment in a clinical department, I recognise the mutual benefits that can accrue from interactions between physiologists and academically orientated clinicians. A similar case can also be made for other scientists with specialised training in areas that have approaches which are valuable to physiology, such as control-system engineers.

My candidacy for Ordinary membership of the Committee is based on many years of active involvement in the Society - this despite having spent the bulk of my years as a physiologist in the United States. I have been a Member of the Society since 1984 and have presented communications at Society Meetings on a regular basis. I have also participated in Teaching Symposia, including editing the textbook which resulted from the symposium on "The control of breathing in Man". With my recent return to the United Kingdom to take the Chair of Physiology at St George's Hospital Medical School, I welcome this opportunity to contribute further to the Society.

#### *Susan Wray*

I am a Senior Lecturer in the Physiology Department of Liverpool University, having worked previously at University College London. I have been a Member of the Society since 1984. I instigated the Smooth Muscle Special Interest Group in 1990 and have just stepped down from being its convenor. I am also a member of the Sub-committee which helps Kwabena Appenteng produce the *Society Magazine*. We are currently working to produce a special issue of the *Magazine* to be given out at the IUPS Congress in Glasgow. I am currently carrying out a survey of untenured physiologists to gain information about their career patterns and aspirations. The results will appear in a forthcoming issue of the *Magazine*. I am also co-organiser of a one day symposium on pH for IUPS with Richard Vaughan-Jones.

I am interested in smooth muscle physiology - particularly uterine and vascular. Along with members of my lab (currently Clare Austin, Louise Earley, Norma Harrison, Richard Heaton, Joanne Phoenix and Michael Taggart), we are trying to elucidate the mechanisms which underlie the fall of force in the uterus during hypoxia. It seems that several mechanisms operate at more than one stage in excitation-contraction coupling (see July 1992 issue of the *Magazine* for more details). It is hoped that a better understanding of how hypoxia decreases uterine contractions may help in the treatment of prolonged labours due to weak uterine action. I am also interested in the mechanism whereby extracellular pH affects vascular tone. Recent work has suggested that the vascular smooth muscle membrane may be particularly permeable to protons.

I have three children, and am thirty something. I would contribute fully to the Committee if elected.



### ***Standing as Officer (uncontested)***

#### ***Richard Boyd - Committee Secretary designate***

I am a university lecturer in the Department of Human Anatomy in the Faculty of Physiological Sciences at the University of Oxford; I am also tutor in Physiology at Brasenose College. Before I took up my present lectureship I was in the Department of Physiology in the University of Dundee (1975-80). I trained in physiology and then in medicine at Oxford and subsequently at University College London and did my PhD on intestinal transport in the biochemistry Department in Oxford.

My current research interests relate to solute transport (and regulation) across epithelia; in particular, the gastrointestinal tract, the kidney and, more recently, the placenta and lung. I am particularly interested in exploiting current developments on the molecular basis of membrane transport to re-examine questions of physiological interest in epithelial transport.

I have been a member of the Editorial Board of *The Journal of Physiology* (and was Chairman from 1988-90), and thus have had experience of the work of the Society's Committee. I would hope that the historical scientific strength of the Society will be a basis for further growth and expansion of the international and particularly the European interactions of The Physiological Society and its sister societies. I am also committed to exploring ways in which the Society can further interact with other UK scientific societies so as to exploit the interdisciplinary excitement of interactions between the many differing strands of modern experimental biology and medicine.

### ***Standing as Designated member (uncontested)***

#### ***Chris Fry - Chairman designate of the Education and Information Sub-Committee.***

All Physiological Society Members would probably agree that a healthy scientific community and a general understanding of science by all are essential in the modern world. However, it is becoming increasingly evident that professional scientists must take a stance on these tenets rather than assume them to be universally shared and understood. Physiology as a discipline is no exception and The Physiological Society is in a unique position to explain to a wider audience what the physiological sciences are setting out to achieve, and to assist those who wish to make physiology and associated disciplines their career.

It is necessary therefore to convince those at school that, for some, physiological science offers an attractive subject to pursue at higher levels and, for others, physiological research makes a positive contribution to aspects which influence all our lives, such as development of medical advances and beneficial drugs. In addition, it is also necessary to convince students in higher education that physiological research and teaching offers an attractive future; to keep teachers at school and in higher education up to date; and, finally, to convince those in positions of authority and influence that a stable scientific - and in particular physiological - base is important for the needs of our society.

Several areas can be highlighted which would fulfil these objectives:

#### ***Schools***

\*To continue and expand visits to schools, along with, for example, the Research Defence Society, to explain what physiology is and what physiological research sets out to achieve. It is important to explain not only to those interested in the

biological sciences but also to provide a balanced argument to others who may receive negative information from various pressure groups.

\*To expand links with agencies such as The Wellcome Trust who are developing interactive scientific centres for sixth formers.

\*To prepare monographs on specific problems which cause problems.

\*To have an input to the GCSE and A level examination boards to co-ordinate better physiological teaching in schools and higher education.

#### ***Undergraduates***

\*To co-ordinate various computer-aided learning projects in the biological sciences, in collaboration with other professional sciences.

\*To continue and expand the symposia on career prospects in the biological sciences, in collaboration with other professional sciences.

\*To discuss the scope and form of practical teaching to undergraduate students.

#### ***Postgraduates and Continuing Education***

\*To initiate workshops for research PhD, MD and MS students on specific topics of more general fields.

\*To improve financial assistance to postgraduate students who might be deterred from following a scientific career.

\*To expand teaching symposia which accompany some Physiological Society Meetings, possibly along with the Special Interest Groups. These are especially important for those in higher education who have to tutor areas other than their immediate fields of expertise.

\*To collaborate more closely with societies in allied fields, such as medicine and surgery, for our mutual benefit.

#### ***Opinion formers***

\*To promote advances made in the physiological sciences in a constructive and informative fashion.

Many of these areas are being tackled at present by the Society and, in particular, the Education and Information Sub-Committee. I would be pleased to chair the Sub-Committee in order to promote the physiological sciences through the areas explained above. I have had previous experience in educational development, especially during the time employed at UMDS. I am one of a group that has been responsible for co-ordinating the recent change in the preclinical curriculum from one based on departmental teaching to a systems approach in which all the preclinical sciences are integrated. Such an integrated teaching approach is also being considered in preparation for the professional surgical examinations and I have been involved in discussions for the preparation of teaching material in this context. In addition, I have been concerned with introducing an element of postgraduate training at UMDS designed to introduce specific and more general topics of interest to research students. My direct contribution to the Society thus far has been as a member of the Grants Sub-Committee.

I would be pleased to assist the Society and the discipline of physiology by acting as chair of the Education and Information Sub-Committee. My predominant research interests lie in the field of muscle cell physiology, but I will endeavour to promote and encourage all aspects of the physiological sciences.



## Committee Members Eligible for Re-election

Name	Years served	Status & Duties	Location	General Scientific Interests
K Appenteng	2	Ordinary member, MASC, EISC, MEG	Physiology, Leeds	Neuroscience, Anatomy & Embryology, Pharmacology
G J Dockray	5	Chairman, Designated (GSC), MASC, PSC, JMG, SP, PPL	Physiology, Liverpool	Gastrointestinal, Endocrines, Neuroscience
A C Dolphin	3	Ordinary member, FASC, GSC, EBM	Pharmacology, Royal Free HMS, London	Biophysics, Neuroscience, Pharmacology
P H Ellaway	2	Ordinary member, MSC, AWSC	Physiology, Charing Cross HMS, London	Neuroscience, Muscle & Exercise, General Physiology
J I Gillespie	4	Meetings Secretary, TASC, FASC, PSC, JMG, PPL, MASC	Physiological Sciences, Newcastle	Cellular & Tissue, Cardiovascular, General Physiology
A Guz	1	Ordinary member, PPL	Medicine, Charing Cross HMS, London	Cardiovascular, Muscle & Exercise, Respiration
C Kidd	6	Ex officio, PSC, JMG, EBM, PPL, AWSC,	Physiology, Aberdeen	Cardiovascular, Neuroscience, Pharmacology
G Leng	1	Ordinary member, TASC, PSC, JMG	Animal Physiology, AFRC, Bafraham	Neuroscience, Endocrines, Reproduction
J M Marshall	3	Ordinary member, MASC, EISC, AWSC	Physiology, Birmingham	Cardiovascular, Comparative Physiology, Respiration
J C McGrath	5	Designated (IUPS), CEC	Physiology, Glasgow	Cardiovascular, Neuroscience, Pharmacology
N G McHale	1	Ordinary member, PSC, EISC	Physiology, Queen's, Belfast	Cardiovascular, Smooth Muscle, Ion Channels, Microcirculation
D J Miller	1	Ordinary member, MSC, SP	Physiology, Glasgow	Cardiovascular, Cellular & Tissue, Muscle & Exercise
D Noble	7	Designated (IUPS), CEC,	Physiology, Oxford	Biophysics, Muscle & Exercise
O H Petersen	1	Foreign Secretary, FASC	Physiology, Liverpool	Biophysics, Gastrointestinal, General Physiology
L H Smaje	1	Ordinary member, SP, PPL, MEG	Wellcome Trust, London	Cardiovascular, Cellular & Tissue, General Physiology
N B Standen	2	Ex officio, TASC, PSC, MEG, SP, EBM, PPL, JMG	Physiology, Leicester	Biophysics, Cellular & Tissue, Neuroscience
R D Vaughan-Jones	1	Ordinary member, GSC	Physiology, Oxford	Heart/Cardiac Muscle, Membrane Transport
J G Widdicombe	3	Treasurer, TASC, PSC, JMG	Physiology, St George's HMS, London	Respiration, Pharmacology, Environmental

### Key:

AWSC	Animal Welfare Sub-Committee	MASC	Meetings Secretary's Advisory Sub-Committee
CEC	1993 IUPS Congress Committee	MEG	Magazine Editorial Group
EBM	Editorial Board for Monographs	MSC	Membership Sub-Committee
EISC	Education & Information Sub-Committee	PPL	Prizes & Prize Lectures Sub-Committee
FASC	Foreign Secretary's Advisory Sub-Committee	PSC	Publications Sub-Committee
GSC	Grants Sub-Committee	SP	Advisory Sub-Committee to Committee Secretary for Science Policy
HSA	Historical Studies & Archives Sub-Committee	TASC	Treasurer's Advisory Sub-Committee
JMG	Journals Management Group		



## Nominations to Editorial Boards

### *The Journal of Physiology*

Name	Location	General Scientific Interests
M L J Ashford	Pharmacology, Cambridge	ATP-sensitive and calcium-activated K <sup>+</sup> channels
E F Barrett	Physiology & Biophysics, University of Miami, USA	Functional interactions between myelinated axons and Schwann cells; mechanisms of transmitter release from motor nerve terminals (electrophysiological and dye-imaging techniques)
J A Boulant	Physiology, Ohio State University, USA	Thermoregulation; hypothalamus; neurophysiology
P B Detwiler	Physiology & Biophysics, University of Washington, USA	Cellular physiology of sensory receptors; sensory transduction; G protein-coupled signal transduction; retinal neurobiology; cyclic nucleotide gated ion channels
S A Edgley	Anatomy, Cambridge	Spinal circuitry controlling movement, and its control by supraspinal descending systems and the cerebellum
M A Hanson	Obstetrics & Gynaecology, UCL, London	Fetal and neonatal physiology; cardiovascular and respiratory control; carotid body and chemoreflexes; baroreceptors and baroreflexes
B H Hirst	Physiology, Newcastle upon Tyne	Epithelial physiology and membrane transport; gastrointestinal tract (secretion, absorption); nutrition and food; liver and bile; microbiology (GI tract); pancreas and salivary glands (and lacrimal glands, etc); mammary gland; protein and enzyme secretion
S C Gandevia	Prince of Wales Medical Research Institute, Australia	Human sensory and motor physiology; control of movement; respiratory muscles; sympathetic nerve activity; neural control in exercise; dyspnoea and respiratory motor control; motor cortex; muscle fatigue (not at biochemical level)
G Leng*	Animal Physiology, AFRC, Babraham, Cambridge	Neuroendocrinology; hypothalamus; endocrines; reproductive physiology; muscular physiology regulation of intracellular calcium
M P Stryker	Physiology, Univ of CA, San Francisco, CA, USA	Central visual system; developmental neurobiology; general neurophysiology; central nervous mechanisms of sensation, perception and movement
J West	Medicine, UCSD, La Jolla, CA, USA	Respiratory physiology, including pulmonary gas exchange, mechanics, blood-gas transport, unusual environments

\*Secretary

### *Experimental Physiology*

Name	Location	General Scientific Interests
J H Mitchell	Southwestern Medical Center, Dallas, USA	Cardiovascular; Muscle & Exercise; Neuroscience
C H Orchard	Physiology, Leeds	Heart/Cardiac; Cellular & Tissue; Muscle & Exercise



## SCIENCE AND THE MEDIA

Articles in this series were commissioned by Saffron Whitehead

In the second series of articles about science and the media Nigel Williams, former science editor for the Guardian, explains the difficulties that scientists are up against when trying to get media coverage. Pat MacCarthy has provided us with an illuminating guide of what to do when approached by the media. There are two articles concerned with COPUS, the Committee on the Public Understanding of Science. This was set up with the prime objective of improving public awareness of science and technology and to bring scientists forward into the public limelight. Jill Nelson briefly describes the background and work of COPUS and Elizabeth Fisher, who was awarded a Media Fellowship by COPUS, gives a scientist's-eye view of the media. Finally, we present examples of press releases prepared from abstracts submitted for the Leicester Meeting of the Society and the coverage these received in the newspapers. Once again we thank everyone for their contributions and hope that the articles in this series may prompt more readers to launch their science toward the media as well as the scientific journals.

Saffron Whitehead

### Daisy's DNA and Dumping Rhetoric

"The press in Britain has never taken science seriously... science news is scrappy and generally operates between the extremes of sensation and the obscure." Thus spoke the crystallographer J D Bernal more than 50 years ago, and although he railed against many things in his later years, I suspect there would be many echoes of agreement among present-day scientists. What is the problem? Why do scientists generally perceive that they and their subject get a poor show in the media?

Sadly, many aspects of the problem have not changed since Bernal's time (and before). Perhaps the key one, particularly strong in the UK, is that of the "two cultures" within the establishment. The term, coined by the scientist-come novelist C P Snow in the late 1950s, simplified yet crystallised a deep-seated gap between those trained in the arts subjects and those trained in the sciences. The media, like most of the professions outside science itself, are dominated by the former. (Curiously, scientists are perceived by journalists as "establishment": often working in government laboratories or with government funds, often on secretive - or unintelligible - projects etc, but this is another problem.)

To take one example, abysmally, less than four per cent of MPs in the last parliament held maths, science or computing degrees. The current parliament looks little different.

I think it is hard to overstate the importance of the lack of representation of at least minimal scientific expertise. The casual ignorance in corridors of power of the significance of scientific theory, the meaning of experimental evidence and the importance of technology can build into an edifice of misunderstanding with the minimum of effort. The odd scientist knocking about the place is not enough.

Snow, in an illuminating vignette, describes in his now-famous lecture on the two cultures the shifty response he once got at a literary party when he insisted on turning conversation to the importance of machine tools.

Science and technology start ten paces back from most other topics before they even get into media attention.

Another surprisingly enduring problem is the power of the anti-science rhetoric. Pitching science against God or against some sort of irreducible human spirituality has done a recent high-profile round following publication in Britain last year of Brian Appleyard's *Understanding the Present*. But scientists are far from squeaky clean in this area in their attempts to embrace "God" within science. Following the success of Stephen Hawking's *Brief History of Time* it is hard not to be cynical about titles such as *The Mind of God* and *The God Particle*. The recent establishment of the Starbridge chair at Cambridge for investigations into links between theology and science (and the media attention it aroused) adds new weight to the issues.

Another potent trick is that of evocation of an older, better, more wholesome past. The rhetoric runs rich. Sir Alfred Ewing opened the British Association meeting 60 years ago with his concern about a "changed spirit" towards mechanical progress: "Admiration is tempered by criticism, complacency gives way to doubt; doubt is passing into alarm. There is a sense of perplexity and frustration, as in one who has gone a long way and finds he has taken a wrong turning. To go back is impossible; how shall we proceed?" Phew.

More plainly, the bishop of Ripon said at the same event a few years earlier: "Dare I even suggest... that the sum of human happiness outside scientific circles would not necessarily be reduced if for ten years every physical and chemical laboratory were closed and the patient and resourceful energy in them transferred to recovering the lost art of getting on together..."

Nowadays the focus has changed but the rhetoric goes on. Bruce McKibben's *The End of Nature* and Rupert Sheldrake's *The Rebirth of Nature* are two recent examples of beautifully crafted scientific gobbledey-gook.

Against this dismally persisting backdrop many things, of course, have changed over the past half century. None less than the media and science themselves.

The advent of broadcasting and development of mass media have drastically changed the "theatre" in which journalism operates. In Britain, at least, there is increasing competition and developments in style, appeal and "popular" journalism with many lessons learned from advertising. At the recent relaunch of the BBC television news formats there was talk of "news branding". Such bums-on-seats approaches present a growing challenge for science.



And science, itself, has developed dramatically over the same half century, mostly moving in quite the opposite direction to the media and getting more difficult and remote with different disciplines finding it increasingly hard to communicate. A recent survey in *Nature* reported a study of the lexical difficulty of science compared with other written and verbal activities, with the reference of 1 given to the level of difficulty in an international English-language newspaper. Top of the league in difficulty were biology papers in *Nature* and *Cell* scoring 40-50; bottom were dairy farmers talking to their cows at -50. The survey gives a measure of the difficulty in translating leading-edge research, particularly biology research, into non-technical, newspaper-level English. And the chance of getting discourse on Daisy's DNA out in the milksheds seems vanishingly remote.

It is also astonishing that science has failed to make more of its real intellectual advances. Sydney Brenner has recently written of how indifferently the discovery of DNA was met by the dominant school of biochemists at the time. Bernal, 15 years

before the discovery, ranked it alongside quantum theory as one of the potential major discoveries of the century. Yet, in the highlights featured in the MRC annual report of the year Watson and Crick made their discovery, all the attention was on the high-altitude experiments (sorry physiologists) carried out on Hillary's Everest expedition.

Finally, in this catalogue of problems, has been the end of the simplistic science and technology as "making things better". Ozone holes, Chernobyl, global warming threats etc are amongst the most dramatic of a number of things that have scuppered the notion of the free lunch, that there can be benefits without costs.

So what is the scientist who would perhaps like to write something for the media or who is faced by journalists to do? The first thing, perhaps, is to take a step back from the bench and look at what you are doing and why you are doing it. Dump the easy rhetoric. Then start thinking about it in words of almost one syllable.

Nigel Williams

## BRITISH ASSOCIATION

*Promoting Science and Technology*

### **Talking Science**

As part of the COPUS/British Association initiative to improve the communication of science to the public, the British Association is setting up a database of speakers on subjects which fall under the broad categories of Science and Technology. The service, currently funded by the Department of Trade and Industry, will be free and available to anyone who needs a speaker on a science subject: a local school might be looking for someone to speak on the opportunities for careers in scientific research; a Women's Institute group might be looking for a speaker to give an introductory talk on science in the home; or a scientific institution might be looking for speakers for a conference on a very specific subject with an audience of specialists. For each such request, *Talking Science* hopes to be able to identify at least one good speaker who can match the requirements in terms of both expertise and style of talk. It is hoped that Physiology will be well represented on this database.

*Talking Science* plans to monitor continuously all aspects of this service, including the speaker's success, in order to ensure that high quality is maintained; ie, this will be, in a sense, a refereed database and *Talking Science* would prefer to receive details of recommended speakers from third parties rather than offers direct from volunteers. If you know of a speaker who has given an interesting, informative or topical talk, the British Association would be glad to hear from you. Please contact Jane Mole, British Association for the Advancement of Science, Fortress House, Savile Row, London W1X 1AB, tel (071) 287 0980, fax (071) 734 1658.

### **Coming Face to Face with the Media: A Practical Guide**

The mass media has an enormous impact on public awareness and it is more important than ever that scientists explain what they do to as broad a public as possible. If science is not promoted and explained, its life force - in terms of new recruits and secure funding - could be diminished.

It is true that journalists do have privileged powers. However, a fact that is often missed by those outside the media and those on the receiving end of journalists' enquiries is that you - the "expert" - hold the real power in the interview situation. Scientists, clinicians and researchers provide journalists with the "wise" and impartial views that put weight and insights into a news piece or forms the backbone of a feature. Without the "expert" for background briefing, comment or supporting evidence, a science story is likely to fall at the first fence. In many ways, the journalists are at your mercy rather than the other way around. In science and health journalism, in particular, facts take precedence over opinion.

If your immediate response to an approach by a journalist is apprehension and mistrust, think again. The vast majority of your contact with journalists will be positive. They need you. But why do you need them? Editorial space or air time on a news or feature programme is worth immeasurably more in terms of credibility than equivalent advertising in the same medium. For the sake of comparison, a simple display advertisement in one of the nationals - across two columns and around ten centimetres in length - could cost you at least £2,000. That helps to put the value of free editorial (probably covering three times as much space) into perspective.

The more readily and widely the benefits of science can be expressed, the more likely it is that public and corporate appreciation and investment will grow. So how do you actually deal with a call from a journalist, remembering that you hold the key to their success? Bear in mind that the majority of interview approaches to you will be by telephone with limited time to meet the journalist's deadline. Here are a few tips to help you make the most of your interview.



## Some DOs and DON'Ts in making the most of the media

### *Before you fix up the interview*

#### **DO:**

- \* Ask what kind of piece or programme they have in mind, what sparked their interest and how they got in touch with you.
- \* Ask if they want background, a quotable comment or an interview?
- \* Stall for time if you want so that you may take advice from your Press Unit, if there is one, or to gather your thoughts.
- \* Always call the journalist back if you have said you will and never say "No comment". It may be used as a quote.
- \* Find out who is actually going to interview you and what sort of angle they will be taking. Talk to them beforehand.
- \* Will they come to you? If so, do you have a suitably quiet, interruption-free room available?
- \* Is the interview to be live or recorded?
- \* If live, is anyone else taking part - who is it and what is their angle?
- \* If there is another interviewee, and it is a radio or TV piece, are you being asked to do a "head-to-head" - ie a debate between you, led by the interviewer?
- \* Roughly how long will it all take?
- \* How much airtime/space will the piece eventually get and in what programme/edition?
- \* When will it be used?

### *Preparing for the interview*

#### **DO:**

- \* Think about your main message and how you will put it across
- \* Think about the questions from the interviewer as openings for you to put across your message and key points.
- \* Write down a maximum of five positive, key points you want to put over that support your central message. These should be short headings just to jog your memory. Never read from a script.

If it is for radio, remember that paper will rustle loudly through a microphone. If you want a memory-jogger and all you have is paper, put the sheet down on a surface where it can be comfortably referred to and don't touch it again. Better still, use a small piece of card for your points and keep it in your hand.

If it is a TV interview, sit slightly forward and breathe easily and deeply before the interview starts. Use your hands, let your face come alive - the camera has a surprising tendency to damp down what you may feel is a really exuberant and possibly even "over-the-top" performance!

- \* Look at the interviewer and not at the camera.
- \* Whatever you do, don't refer to "listeners", "viewers", or "readers". This comes across as rather grandiose and a bit patronising and won't win you support!

\* For all of the media, but especially for pre-recorded radio or TV, try to talk in "stand-alone sentences". For example, if someone asks you what you had for breakfast, rather than saying: "Eggs and ham" which they cannot use as a clip on its own, it is better to say: "I had eggs and ham for breakfast". This may seem slightly odd at first, but it does mean that your interview will be easy for them to use and will therefore be more likely to get on air.

\* Try and make the journalist's job easy. People everywhere love dealing with other people who make their jobs easier and journalists are certainly no exception!

\* Remember, if you look as though you believe what you are saying, your confidence and credibility will increase exponentially. Keep your own pace and personality, and above all - **be positive!**

The interview is not a form of torture - it is a valuable opportunity, and one that you can thoroughly enjoy!

#### **DON'T**

\* Worry about rehearsing answers to sticky questions. The best way of being prepared for awkward questions is to be sure about your message and your supporting positive points. You may want to look up a few relevant facts and figures to quote, but just a few!

\* Worry too much about how you look or sound: if you follow the "Do" points above, the rest takes care of itself.

\* Let any of the mechanical recording paraphernalia, or presence of a crew, put you off. Ignore them. The crew simply want to get on with their job, they are not making any judgements. And the machinery is simply the means for you to ultimately reach an audience.

### *Structuring your interview*

All you need is the clear central message as your beginning, the handful of positive supporting points as the bare bones of a middle, and the summing-up of these at the end.

### *The beginning*

#### **DO:**

\* Get the beginning of the interview right because this is the point at which you set the tone of your interview.

\* Take control and make your own point, rather than letting your response to the opening question put you on the defensive from the start.

\* Briefly state your key message in your opening statement. Clearly it will be in response to the interviewer's first question. No matter how specific or even negative the question to you may be, using your key message as an opener does work - as long as you are succinct and positive.

For example: your key message may be the value or uniqueness of the work done by your institution. Say, for example, this work is costly and your funding may be under threat. Sounds familiar?

Question: "X has to be one of the most costly higher education courses in the country per student. You take in only Y students every year - wouldn't the funds be better spent in enabling more students to take up less cost-intensive degree courses?"



**Your Opening Response:** "X trains 90% of the UK x-ologists, without whose work Z could not happen." (Add very brief example of value of the institute's work to the wider public...) "The teaching is highly technical and tutor-intensive, but the skills and research from X are recognised world-wide because of their consistently high quality. It is a national resource that deserves proper investment" - ie: Stick to your message and the positive things that are happening.

### **The middle**

#### **DO:**

- \* Continue to make positive and factual statements based on your key points. Don't abandon your ideas or your positive points during the body of the interview, particularly if there is another interviewee involved who starts drawing the debate down paths which you do not wish to follow.

- \* Try to be as concise as you can throughout, without losing your own personality or pace. Most interviews last only a short time - especially radio and TV - and the final edited version of a pre-recorded interview is cut down to even less.

#### **DON'T:**

- \* Ever expect to be able to work from a "script" in an interview!

It is never done. This is not because anyone is trying to push you into unknown territory or to catch you out. The truth is, it is very obvious when someone tries to read from a prepared statement - it looks and sounds appalling - and, worse than that, it seriously diminishes your credibility!

- \* Waste time by using phrases like: "As I said before..." as the previous comment may be edited out, and that would make the phrase above unusable.

- \* Ever say "No Comment"! Unless you are being chased out of a court-room (God forbid) and matters are sub-judice - in which case you are clearly justified in refusing comment - this phrase is not to be used. It always sounds tremendously guilty and evasive and, if subsequently used by the journalist as your only response in a story, it actually reinforces any potentially negative slant!

If a matter has yet to go before a public committee within the University then this is a reasonable excuse for being unable to help the journalist at that point.

If you need time to think about a specific question and the interview is not live, you can promise to get back to the journalist "after checking one or two details". Where possible, do stick to your word and call them back!

### **The end**

#### **DO:**

- \* Always try to finish off by returning to your original message and reiterating it. Briefly sum up your positive points if there is time. Maximum: two sentences.

- \* After the interview is over, if you have been involved in a reasonably lengthy pre-recorded broadcast piece (several minutes), you might wish to ask the interviewer if they can send you a copy of the final version that is broadcast. This is a good thing for you to keep anyway, but also indirectly underlines to them - should it be necessary - that you are keen to keep tabs on how your words are finally used!

- \* If getting a copy is a problem, for whatever reason, make sure you at least know the likely time of broadcast so that you can record it!

*Pat MacCarthy  
Media Relations Officer, University of London*

## **COPUS: Improving Science's Public Image**

Science and technology affect the lives of everybody, whether or not they are professionally involved. Some scientific awareness, such as how diseases spread by germs, is just plain useful in everyday life. In an industrial democracy dependent on science and technology-based industry, there are things that people should know about to reach informed decisions on the issues of the day. Many of these issues, such as the Greenhouse Effect and the spread of AIDS, require some degree of scientific literacy to reach informed decisions. Better public awareness and understanding of science can be a major element in promoting national prosperity. Science and scientific curiosity are also part of our cultural heritage handed down through the generations.

More and more scientists are beginning to see the merits of explaining their work to the public. Many are finding that communicating science can be a rewarding and pleasurable experience if gone about thoughtfully with imagination. The Royal Society's Bodmer Report, COPUS, was established by three of Britain's oldest scientific institutions, the Royal Society, the British Association for the Advancement of Science and the Royal Institution. Membership is drawn from the three founder institutions and from a number of groups involved in promoting science, such as the education system, industry, government, the media, museums and science centres, press and broadcasting, and the scientific community. The Committee initiates and

organises its own activities, which are run by the three founder bodies. In addition, COPUS acts as a central forum for other organisations active in the public understanding of science, plus helping to maximise the use of limited available resources.

Many individuals and organisations inside and outside the scientific community feel that the behaviour and attitude of scientists in the past has alienated a large sector of society. COPUS recognises this and realises that it is the scientists themselves that can do the most to raise the public understanding of science. Because of this, engaging the direct support and involvement of the scientific community remains COPUS's highest priority and the Committee is working in a number of ways to encourage and facilitate activities.

Activities and initiatives for scientists and engineers include encouraging them to communicate widely through the Media Fellowships Scheme, media training workshops, and liaison with public relations officers in research institutions and leisure places, Parliament and Government, industry, the City, women, voluntary and special interest groups and provide grants through the Royal Society for public understanding of science projects.

*COPUS Looks Forward: the next five years*, and other information, is available from the COPUS Secretariat, c/o The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG, tel (071) 839 5561 Ext 219.

*Jill Nelson  
COPUS Executive Committee*



## Working with the media: the Media Fellowship Scheme

There is a war going on quietly in Britain today. It's a guerrilla war. It's being waged without obvious guns and mortars, but the effects are plain to see - destroyed manufacturing industry, low economic growth, a population which trusts in homeopathy and crystals, decreasing numbers of numerate children and growing hostility towards science. Dark Ages - the re-make. Who are the chief protagonists? On the side of the New Ignorance are such luminaries as Brian Appleyard, Fay Weldon, Mary Kenny, the entire British population of accountants and all my friends who work in the City. On the side of Truth and Enlightenment and Humanity are... us. And we are losing.

Do you agree? You're sitting there thinking "she's a weirdo, but maybe there's a grain of truth in it" and you're imagining yourself out of the lab coat and specs and into combat fatigues and contact lenses. Well, I only wrote the first paragraph to capture your attention. That's one of the first things you learn about media writing. Of course, actually I *believe* all of the above which is what prompted me to apply for a British Association Media Fellowship last summer.

I run a group studying the Molecular Genetics of Down's syndrome at St Mary's in London. Last year I spent eight weeks working full-time with the Science Unit of the BBC World Service in addition to trying to run my lab - full time. Why do people put themselves through this kind of experience, trying to side step the space-time continuum? I had three main reasons. Firstly, I believe a large number of our ills have arisen because this country does not take science and maths seriously. It is suspicious of these disciplines and so has deserted technology and opted for the service industries instead. Service industries are cool. Everyone can grow a pony tail, drive a company car and be Jason from Sales or Amanda from Marketing - where technology extends as far as the espresso machine (Italian) or the video screen (Japanese - for the midday financial news and afternoon children's programmes). Northern chemists only for the manufacturing industries.

Well, we get what we deserve. Britain has more accountants per capita than any other country in the world. Meanwhile, Britain's scientists and technologists work under conditions deemed unacceptable to other professionals and at pay levels often below the national average, and well below the average for our educational status. When I read my very red bank statement and check my legendary credit card bills I'm left screaming in frustration that my neighbour's 19 year old secretary earns more than me. Scientists as a group are not very good at asking for more. This genteel disdain of fuss has cost us our status, our ability to attract students, our credibility and some people their jobs. Scientists need to be seen more, seen as real human beings and not soap powder advertisement stereotypes. We need to make more noise.

Secondly, we have an obligation to our ultimate employers, the charity donor and the tax payer, to explain what we do. Society needs the ability to make informed decisions, particularly in a field like mine, genetics. Science is a source of inspiration and

hope and we should communicate the excitement of science to the people who pay for it. Without their support we cannot continue - and their lack of support is evident.

My third reason for applying for the Media Fellowship was probably the most important reason. It looked fun. Two months seems a long time to be (half) out of a lab, which is why few academic scientists seem to apply I'd guess. But the Fellowship is an utterly brilliant scheme to get working scientists into the media - correcting our image, correcting their writing. It's like having a baby, dearies, there is never a good time so you may as well try it out now. (I don't have a baby but I'd like to thank my mother for the advice.)

I was extremely fortunate and went to work with John Newell and his Science Unit at the BBC World Service. The science writers in the unit are not only highly skilled reporters with great integrity, but also skilled scientists - a large number had PhDs. I was totally impressed and so - disappointingly - I had nothing to grumble about. I was taught to assimilate and write a large number of reports and articles and felt more up to date with all aspects of science than I have since taking A levels. I had the thrill of broadcasting to the awaiting world. An appreciative world which values science and listens to cosmology and molecular biology with ears extending from tiny African hamlets to Polynesian villages. During the course of my Fellowship I began to learn the editorial process which afflicts the media, mainly newspapers. This is the process by which a non-scientist (the editor) is in charge of what is printed. Therefore, however much is written by science reporters, only a very limited amount will be published. This accounts for why all non-tabloid newspapers publish column miles of Arts pages on arcane productions of Genet in Surbiton and all tabloids publish news of the Royal Family only. Clearly, if Prince Charles became a research chemist interest would cease immediately and the paparazzi would return to photographing motorway pile-ups.

Editors are in charge and most of them firmly believe we want to read about anything but science. Dog shows, horoscopes, Patagonian nationalists, anything but the one force which is irrevocably changing our lives. Science has few media Heros. David Attenborough? Stephen Hawking? Very few - even Clark Kent was a journalist. There are many Media detractors of science but our worse enemies are ourselves. There is a strong ethos in British science which says it is nothing but perverse and ostentatious self-gratification to want to communicate and popularise. Serious scientists should have their eyes down and stick to being part of the intelligentsia.

I'm a normal working research scientist. I enjoy the intellectual life of science and the practical life of the lab but I also want to popularise science. The Media Fellowship Scheme is an excellent way to take your skills and knowledge and use them to make science more accessible and less threatening. It is one way of giving back to Society and safeguarding our future at the same time. There are other ways - contact COPUS and help out. Go and give talks about physiology in schools, go and tell the local Mother & Baby group about quarks, even take time to explain super string theory to your irritating nephew. We are aiming for a more educated population, a healthier economy and the right to shop in suburban High streets without nasty encounters with zoned out Animal Rightists ("AIDS is a CIA plot - the Americans brought it back from the moon." Kensington High Street, c April 1992).

*Elizabeth Fisher*



## Increasing the accessibility of abstracts -

### step 2: identification of abstracts of general interest and preparation of press releases

The last issue of the Magazine contained two versions of the same abstract, one written for an audience of physiologists and the other written for a more general audience. The next stage in the experiment has been to identify, from the abstracts submitted for the Leicester Meeting, those which contained material of general interest to a lay audience. A specialist firm of science writers were then asked to prepare, in conjunction with the Meetings Secretary and the authors, press releases of these abstracts. Ten potentially suitable abstracts were identified but these were eventually whittled down to just four. Two of the releases were subsequently used as the basis of articles in newspapers. The two releases are reproduced below, together with some of the press cuttings based on them.

## Breast-Feeding Protects Babies

(Source - Poster Communication 15)

Mothers were told today by scientists that there is no doubt that "Breast is Best". They have discovered that bottle-fed babies may not produce enough acid in their tummies to kill off harmful bacteria.

Every year millions of babies around the world become ill, and many die because of infectious diarrhoea. The risk of infection is higher among babies on infant formula milks than among those who are breastfed.

Research findings announced at The Physiological Society's Meeting in Leicester show that one reason for the increased risk is that the gut of the bottle-fed babies is less acid.

In particular, it contains less acetic acid (vinegar) and less lactic acid, produced by protective bacteria, which stops harmful bacteria multiplying.

In addition the lower iron content in breast milk may help promote the growth of protective bacteria.

The research was carried out by Dr Christine Edwards and colleagues at the Department of Human Nutrition, Glasgow University, Yorkhill Hospitals, Glasgow, and at the Milk Bank, Sorrento Maternity Hospital, Birmingham.

Dr Edwards, lecturer in human nutrition at Glasgow University, said: "Breast feeding is definitely best but very few mothers maintain breast feeding for very long and some never even start. 60% of mothers leave hospital breast feeding but that declines quite quickly."

A spin-off from the research is that it may help infant formula manufacturers change the formula so that products are closer to the real thing.

Note: Previous research shows that breast feeding during the first 13 weeks of life confers protection against gastrointestinal illness long after the period of breast feeding.

## Scientists insist: Breast is best

MOTHERS were told today by scientists that there is no doubt that "breast is best".

New research shows that bottle-fed babies may not produce enough acid in their tummies to kill off harmful bacteria.

Acetic acid and lactic acid, which are produced by protective bacteria and stop the dangerous bacteria multiplying, are found more in breast-fed babies.

The lower iron content in breast milk may also help to promote the growth of protective bacteria, according to researchers in Glasgow

by Jo Nevill

and Birmingham, who spoke today at the Physiological Society's meeting in Leicester. Dr Christine Edwards, lecturer in human nutrition at Glasgow University, said: "Breast feeding is definitely best, but very few mothers are able to do it for very long - and some never even start."

Previous research has shown that breast feeding during the first 13 weeks of life gives protection against gastrointestinal illness long after the period of feeding. Studies have given

conflicting advice in the past as to how good breast feeding really is for babies. Last year, research showed that boys who were fed for more than a year were more likely to suffer from heart disease in later life.

Other research has suggested that the fatty acids in breast milk give babies 10 and 20% weight advantage over bottle-fed infants.

It is not known, however, whether this is the hormone in the milk itself, or the act of suckling, which is important for development.

Britain has one of the lowest rates of breast feeding in Europe.

## Heart Concern Over Anti-Smoking Aids

(Source - Oral Communication 76)

Nicotine anti-smoking aids may increase the risk of heart disease if used for excessively long periods, according to new research presented today to a Meeting in Leicester of The Physiological Society.

Thousands of people are currently on nicotine replacement therapy, either chewing nicotine gum or applying nicotine patches as an aid to stopping smoking. But, while the therapy is much safer than smoking, new evidence suggests that nicotine, in whatever form it is taken, significantly alters blood circulation within the arteries.

Researchers are now working on the theory that these changes may contribute to arterial disease, thereby increasing the risk of heart attacks and strokes. The research by medical student Chris Rees, Professor Colin Caro and Mr Nick Watkins of the Centre for Biological and Medical Systems at Imperial College, London, involved giving Nicorette chewing gum and a placebo version to healthy young volunteers.

Ultrasound scans of the main artery of the thigh showed significant short-term changes in blood flow pattern and stiffening of the artery wall soon after the volunteers started chewing the gum. These changes were similar to those induced by cigarette smoking.

Professor Caro said the changes included a speeding up in the rate of blood flow. As with rivers, this might increase the risk of stagnant pools forming along one "bank" of the artery when it turned a corner. Fatty deposits could then start building up, increasing the risk of arterial disease. He added that a larger study, funded by the Tobacco Products Research Trust, was now planned to confirm the findings. "However, there is concern in the case of people who become addicted to the gum, particularly if they already have a heart condition or angina".

Mr Rees, who carried out the research as part of a Bachelor of Science project, said gases such as carbon monoxide, absorbed during smoking, were widely believed to be responsible for the known link between smoking and arterial disease. The new findings suggested that nicotine might be at least as important, if not more so. The exact mechanism involved has still to be identified, but the researchers suspect that one element is nicotine's action in stimulating the release of the "fight or flight" hormone noradrenaline, which causes the heart to beat faster and the arteries to become stiffer.

As far as nicotine replacement therapy is concerned, Mr Rees said: "The idea is to wean people off cigarettes. I can't say that is a bad thing because they are not receiving carcinogens from the smoke. But maybe there should be health warnings on the packs about heart disease if our theory is correct".

From the Evening Standard



# Peril of the patches

## NO-SMOKING AIDS 'ARE HEALTH THREAT'

Anti-smoking aids that need a health warning

NICOTINE anti-smoking aids could increase the risk of heart disease if used for long periods, researchers warned yesterday. Thousands of smokers are using the aids to quit the habit.

## Nicotine patch heart danger

Research pinpoints blood flow changes

NICOTINE anti-smoking aids could increase the risk of heart disease if used for long periods, researchers warned yesterday. Thousands of smokers are using the aids to quit the habit.

NICK NU  
TECHNOLOGY  
CORRESPONDENT

PEOPLE who try to quit smoking by using nicotine...

Health warning over using nicotine patches

By ALAN MACDERMID  
Medical Correspondent

SMOKERS who use nicotine patches...

'Risks' of anti-smoking aids

NICOTINE anti-smoking aids could increase the risk of heart disease if used for long periods, researchers warned yesterday. Thousands of smokers are using the aids to quit the habit.

## Nicotine patches raise heart disease concern

SMOKERS who use nicotine patches or gum to help them give up cigarettes may continue to risk heart disease, researchers warned today, writing...

## 'Heart risk' from nicotine gum

NICOTINE anti-smoking aids could increase the risk of heart disease if used for long periods, researchers warned yesterday.

Fears raised on Nicotine chewing gum may increase heart risk

NICOTINE anti-smoking aids could increase the risk of heart disease if used for long periods, researchers warned yesterday. Thousands of smokers are using the aids to quit the habit.

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Prof Colin Caro showed significant short-term changes in blood flow pattern and stiffening of the artery wall. Those changes were similar to those induced by cigarette smoking. Prof Caro said the changes included speeding up in the rate of blood flow. As with...

Cuttings taken from: the Daily Express, the Daily Mail, the Glasgow Herald, the Guardian, the Independent, the Liverpool Echo, the Northern Echo, the Scotsman, the Star, the Times, the Yorkshire Post

## Retiring Committee Members

The six members of the Committee retiring at the AGM were each asked to discuss the issues they would like to see tackled or resolved by the Committee in the next few years. David Eisner's contribution appears in the Letters section and a series of articles on the theme of his letter will appear in the September issue of the Magazine. Humphrey Rang and John Kemp (the latter together with Leslie Iversen) took as their theme the importance of establishing closer contacts between research workers based in universities and in industry. University based researchers are sometimes unaware of the importance of physiology in pharmaceutical industry research. To help counter this, Humphrey Rang has provided a succinct overview of the opportunities for physiologists in the pharmaceutical industry. John Kemp and Leslie Iversen follow this with a picture of how interdisciplinary research is carried out in a major pharmaceutical company. Peter Campbell, chairman of ARMS (Association of Researchers in Medicine and Science) then gives a more general overview of the current debate on the question of career opportunities for research scientists. [The theme is one which we will return to in a later issue of the Magazine, when Susan Wray will report on the results of a survey she has undertaken of the career aspirations of untenured staff in departments of physiological science. Questionnaires, together with stamped addressed envelopes, have been sent out to 1,095 untenured staff, their names and addresses having been provided by department heads. We hope Members will encourage all those who have received questionnaires to complete and return them to Susan Wray.] The contributions from the three other retiring Committee members took the form of interviews, all of which will appear in the September issue of the Magazine.



Left to right: Richard Dyball, outgoing Secretary of the Editorial Board of The Journal of Physiology; Linda Barrett, Personal Assistant to the Committee Secretary; David Eisner; David Cotterrell, outgoing Committee Secretary; John Atherton, outgoing Chairman of the Education & Information Sub-Committee.



## CAREER OPPORTUNITIES FOR RESEARCH SCIENTISTS

### Opportunities for physiologists in the pharmaceutical industry

A scan through the first 100 Ordinary Members in the Society's Grey Book reveals only two with "industry" addresses (in the British Pharmacological Society Handbook there are 28). This low number may have something to do with the Society's election procedures in the past; whatever the reason, it suggests that the nature of pharmaceutical industry research, and the relevance of physiology to it, may not be all that clear to many Physiological Society Members and, perhaps more importantly, to their students. Having moved into industry about eight years ago, after a very conventional academic career, I think I understand quite well the similarities and differences between these two worlds. In this article, I will focus on just a few aspects, concentrating on those which may particularly concern a young physiologist who is making a career choice. The details reflect my own experience at Sandoz; they are fairly typical, but companies are not all the same in their scientific policies and practices.

#### *The purpose of research*

On the face of it, the purpose of academic research is to add to human knowledge through the medium of scientific publications; whereas, in a pharmaceutical company, the purpose is to discover new drugs, which can be developed and sold at a profit. This basic difference will always exist, but is tending to become less distinct, as academic researchers are increasingly encouraged to commercialise their discoveries as a way of supporting the cash-starved academic endeavour, and as wealthy pharmaceutical companies plough resources back into academic research in a somewhat altruistic way. At bottom, though, academic research measures success in terms of publications, whereas a pharmaceutical company's research is judged by the number and quality of the development compounds that it discovers. The difference is important, and has wide implications for the way in which the research is organised and managed, but the relative advantages and disadvantages of the two environments for a working scientist are, to my mind, quite evenly balanced. It takes wits just as sharp, and techniques just as good, to succeed in the drug discovery environment, as in any other field of research.

#### *What about academic freedom?*

A major concern for many scientists is that a career in industry will entail the loss of something very important, namely the freedom to pursue whatever line of research one chooses, to communicate freely with other scientists, and to submit for publication what one pleases. There is the fear that the company will exert such tight control over their work that the creative spark, as well as the outside recognition that goes with publication, will be lost. Where the truth lies on this important issue varies a good deal from company to company, and even in different parts of the same company. Companies of course exert more control than academic institutions over the general direction of their research activities, the latter being heavily dependent on the grant-pulling power of their individual scientists. The

constraint imposed by management decisions within a company is not, however, so different from that imposed by the need to impress outside granting bodies. When it comes to getting approval for interesting projects, there is, in my experience, not much to choose between academia and industry; grant-giving bodies, like company managements, can seem visionary one day, and myopic and prejudiced the next. The main difference is that industry makes up (and may change) its mind much more quickly, which can be disconcerting to one used to the more stately rituals of academia.

Freedom to publish is necessarily restricted in a company environment, since prior publication precludes patent cover for discoveries. This legal fact means that formal permission is always needed before work can be published. Different companies nevertheless vary greatly in their approach to publication; some encourage it to the maximum extent that does not compromise their patent position (and even require it as criterion for promotion), whereas others tend to be secretive by nature, and reluctant to publish for fear of helping the competition. Often, studies describing new and promising compounds will be embargoed until development is well advanced or the project is abandoned. Basic research that is not concerned with development compounds can, however, be published, and in most companies, there is little problem or delay in getting the necessary permission. Enlightened companies recognise that communication with outside scientific groups brings many rewards, and that they need to be open as well as receptive in order to benefit from it. The best way to judge a company's attitude on this issue is to ask to see its publications list.

#### *How are decisions made?*

All companies have a more or less formal process for reviewing potential projects, taking into account such factors as the perceived chances of success in producing a development compound (and maybe of beating the competition to it) and the resource requirements, as well as the attractiveness of the science. Once a project is approved, a project leader is appointed, resources are allocated to it (usually less, needless to say, than the project leader would like), and the team is generally left to get on with it, with a progress review every six months or so.

In companies where preclinical research is organised into topic-related departments (eg cardiovascular research, CNS research, etc) - the majority nowadays - decisions about new and continuing projects will generally be made at the departmental level. Criteria vary greatly. Some departments take a hard line, and will approve projects officially only when the underlying biological idea has been clearly established, when a clear chemical starting point has been identified, and when a smooth-running assay system has been developed; from there on, the project is essentially a matter of refining the chemical structure until an acceptable pharmacological profile is achieved. Others initiate projects to try to establish a good biological basis for a later drug discovery effort; they might, for example, wish to clone an enzyme or a receptor, to study its distribution and regulation in the body, and investigate its possible relevance in a disease process. Then, if the pieces fall into place, they might set up a chemical screening programme to search for a chemical lead, before initiating a programme of chemical synthesis and testing aimed at producing a drug for development. Research at the exploratory phase of a project like this is often indistinguishable from the kind of project usual in academia; the team will generally be small, the ideas and objectives will be



self-generated, and research managers realise that ideas come mainly from individuals who are given the time and resources to follow their curiosity. At the Sandoz Institute, our policy is for all scientists to be given 20% of their time to work on anything they like so long as it is not excessively expensive or smelly.

At intervals of 6-12 months, a higher level research committee will review the overall work of the department, and may direct it to make large or small changes, such as closing down projects, reallocating resources between projects, or opening up a new research area. A CNS department, for example, working on epilepsy, might be directed to stop a project on GABA agonists, and start instead on the glycine receptor, or on a completely different project, such as analgesic agents. For the individual researcher, who has committed a great deal of time and effort to a project, decisions like this can be extremely frustrating, however persuasive the commercial case may be, and it is probably this aspect of corporate life that is least acceptable in the eyes of many aspiring scientists. Good research managers understand this and avoid sudden changes of direction. Bad ones, on the other hand, seem to think that the reluctance of project teams to change direction every Friday, when *Nature* arrives, signifies indolence and complacency, and calls for tough managerial direction. In a company, individual managers generally have more influence (good or bad) over their departments than, for example, a university professor, and they tend to change places more often. In general, the pace of change is greater in industry than in academia, and it is less predictable. This is because there is less constitutional stability - no Academic Board, with statutory procedures, etc; in a company, a few key individuals make and change policy as they see fit, and the consequences can be rapid and far-reaching.

#### *How do companies organise research?*

Pharmaceutical companies vary in the way that their drug discovery research is organised. Most now have topic-related departments (eg cardiovascular research, gastrointestinal research, CNS research, etc) in each of which several scientific disciplines are represented (eg chemistry, cell physiology, whole-animal physiology, pharmacology, molecular biology, etc). These departments are normally backed up by a range of "service departments", covering some of the high-tech functions such as molecular modelling, high-throughput compound screening, transgenic animals, computing, protein sequencing, etc.

The most important unit is the Project Team, consisting of the group that actually does the work: teams may vary in size from five or so scientists to 100 or more; they frequently undergo creation, expansion, contraction or dissolution, depending on current priorities. These teams are always multi-disciplinary, consisting typically of chemists, biochemists, physiologists, pharmacologists, molecular biologists, etc. Quite commonly, an individual scientist will belong to more than one such team. Such teams, collaborating on a single project which has been planned from the outset as a collaborative effort, can be very impressive in finding their way round problems because of the range of different approaches they can bring to bear. Disciplinary boundaries, of the kind that are often so frustrating in academia, can be ignored. Collaboration within such a team is obligatory, not discretionary, and this makes a big difference.

Since the project teams are the main vehicle for discovery, ability to work effectively in such teams is essential. In such a group, particularly a large one, a lot of effort needs to go into

communication, partly through written reports and partly through frequent project meetings at which results are presented and discussed, and future plans are formulated. Most pharmaceutical company scientists grumble about the amount of time they have to spend writing and reading reports, and attending meetings, just as academics do about "administration". Even the best scientists may find the process of communication exasperatingly difficult, and feel most comfortable working on their own with the door shut. If this is your style, working in the pharmaceutical industry will not suit you. My advice is: if you like the challenge of trying to make someone *understand* what you think is important, come right in! If you find having to explain yourself to a non-expert an irritating distraction, think again.

Though working in a project team requires additional effort, and more discipline, compared with an average laboratory-based academic group, the rewards are certainly greater in terms of the progress that can be made, once the goal is clearly defined. Some scientists undoubtedly find it hard to adjust to the project-team mentality after having worked independently in a small academic group, but most welcome it. There is less evident tribalism than one commonly finds in successful academic groups, but no less sense of achievement when things work out. In industry, scientists run up and down corridors, lean anxiously over the scintillation counter, covet their special tricks and gadgets, and generally experience the same joys and frustrations as they do anywhere. The size of project teams in industry can undoubtedly lead to problems over authorship - particularly *first* authorship - when it comes to publication, but this is also a familiar minefield for collaborative projects in academia.

Invariably the project will have a clearly-stated goal, and will also include a set of short-term objectives and time-limits. For example, the goal might be to identify a new potassium-channel opener that acts selectively on airways smooth muscle. The objectives for the first year might include: set up airway and vascular smooth muscle preparations and binding assays for potassium channel openers, and test a panel of existing compounds for possible selectivity; set up patch-clamp technique for characterising potassium channels in different types of smooth muscle; isolate and purify the relevant binding protein from different sources, including airways smooth muscle. Setting up such long and short term objectives usually involves a lot of discussion and argument, but it is essential that they are fully endorsed by the whole research team at the outset, for they set out the route, and also provide the milestones by which progress is measured; if the project goes off track, or progress is too slow, it may well be stopped. With an average MRC project grant, the objectives for three years of work are usually drafted by one person a year or more in advance, and, in my experience, seldom referred to again. The grant application sets out the general direction at the outset, but often a more favourable avenue opens up, and the project achieves something quite different from what was envisaged. So long as the work is good, and the results publishable, everyone is happy, for what matters is publication in a good journal, rather than the solving of a particular problem.

What a scientist cannot easily do in a company environment is to build a private fiefdom, based on successful grant applications. In academia, the size of an individual's research group, the amount of space, equipment and grant income he can attract, are often the measure of his success and achievement. In a drug company, resources generally follow the project, rather than the individual scientists and his group. Some scientists find this hard to accept, but many find working within a successful



multidisciplinary team more fulfilling than struggling to meet the requirement of academia that they should build and sustain an independent group. The choice, for the individual, is an important one, and unfortunately many seem to get it wrong. If what you care about is to be a high-profile scientific entrepreneur, it would be best to avoid a job in industry - or maybe start your own company.

### *Career prospects*

Many pharmaceutical companies recruit graduates in biological science or chemistry as scientific assistants; some have a large non-graduate workforce for routine laboratory procedures, but in others all of the scientific work is done by graduates. Some, including the Sandoz Institute, allow graduate scientists to work part-time towards a PhD. At Sandoz, they continue to work in the same laboratory, with no change in pay or promotion prospects, and with the same supervision, but are registered with an external academic supervisor who shares responsibility for their PhD-related project work. An internal "PhD committee", to whom the student reports regularly, is responsible for monitoring progress. PhD work is normally kept separate from routine duties, and is expected to occupy about two days per week, plus spare-time study. Completion of a PhD should be possible in five years under this scheme.

PhDs with postdoctoral experience are normally recruited as Senior Scientists or Laboratory Heads, who will be responsible for a laboratory with perhaps two or three junior staff (graduate assistants, sandwich students, etc) to supervise. The next level is generally the Section or Department Head, responsible for the work of related laboratories.

The role of Project Leader usually falls outside these line management positions. At Sandoz, it is an additional duty often taken on by the scientist who has been the prime mover in initiating the project, but in other companies it may fall to more senior managers. It is in many ways the most challenging and satisfying function, since the Project Leader's task is to get a multidisciplinary team, including, usually, some gifted prima donnas, functioning as a coherent unit. To do it well, the Project Leader has to stay abreast of everything that is going on, including what lies outside his field of expertise, to keep the objectives firmly in view, and to have considerable gifts of persuasion, since multidisciplinary teams have a strong tendency to rush off in all directions. The job calls on skills that owe little to scientific training.

Most pharmaceutical companies employ temporary as well as permanent staff. These include: summer vacation jobs for undergraduates (strongly recommended as a way of learning whether the environment suits you); sandwich student placements, usually of one academic year; PhD studentships, either based full-time in the company's research laboratories, or as part of an academic/industrial co-operative; and postdoctoral fellowships of one to three years. Vacation or sandwich students will often be involved in ongoing project-related work, and gain valuable experience of laboratory discipline and procedures; they will usually work on their own projects, as well as participating in routine work. PhD students and postdoctoral fellows are able to work on their own projects, the aim being to produce published work, rather than contributing directly to drug discovery projects. They are valuable to the company because they bring in new ideas and techniques, and allow free-ranging exploratory work to go on alongside more directed projects. At the same time, they gain experience of applied

research, and can decide whether or not it suits them. It is a mistake to expect that a limited-term fellowship will automatically lead to a long-term position with the company; usually, this is not the case.

Some pharmaceutical companies operate a "dual ladder" career structure, which enables productive scientists to achieve promotion without moving away from the laboratory. Alternatively, they may be able to move on the "management" ladder, taking on greater responsibilities, but at the expense of direct involvement in laboratory work. In fact, it is very common for junior scientists, particularly those without a PhD, to move out of laboratory science after a few years, into junior management positions, for example, in clinical trials management, regulatory affairs or marketing. The major international pharmaceutical companies are very large organisations, with thousands of employees around the world, so the opportunities for career moves are considerable. The nature of their business means that a good training in biological or medical sciences is always a considerable asset.

### *What can a physiologist contribute to a drug discovery research team?*

"Physiology" has become an extremely broad discipline, covering the whole spectrum from molecular to whole animal studies. This breadth of view - which physiology teaching needs to preserve at all costs - is extremely valuable in the drug discovery process, where the leads often come initially from a molecular approach, but have to be followed through to discover what is going on at the level of cells, tissues, organs, whole animals, and often disease processes. In fact, one of the problems that the industry faces is that broadly-based physiologists and pharmacologists are becoming scarce as fashions have swung towards molecular and cell biology. New whole animal techniques, such as imaging and remote sensors, have enormous potential for the pharmaceutical industry.

I hope that this article may have encouraged young physiologists thinking about career choices to give consideration to the pharmaceutical industry. Their skills are certainly needed there, and it can offer challenges, opportunities and rewards that are hard to find in academia. Maybe in time we shall find a few more drug company addresses in the august pages of the Grey Book. The fact that there have recently been two such among The Physiological Society Committee Members is surely a good start.

*Humphrey Rang*

### **POSTGRADUATE SUPPORT FUND**

Support for postgraduates in exceptional circumstances such as periods of ill-health, absence of essential facilities, disruption of supervision etc, to assist in the completion of their research projects and to bridge the period between graduation and the availability of full-time posts for especially gifted students.

**Eligibility:** Graduates in physiology, or a cognate science, engaged in research in the UK in a department of Physiology or cognate science, when their supervisor is a Member of The Physiological Society. Applicants will normally be registered for a PhD, although MPhil and MSc students may apply.

**Awards:** The maximum award allowable will be £1,000.

**Application forms** are available from the Society's Administration Office, PO Box 506, OXFORD OX1 3XE, tel (0865) 798498, fax (0865) 798092.



## The Neuroscience Research Centre, Merck Sharp & Dohme Research Laboratories, Harlow, Essex

The Neuroscience Research Centre started ten years ago and is responsible for all research on nervous system diseases for the parent company, Merck & Co. We moved into our modern laboratory complex near Harlow in 1984 and there are now in excess of 160 graduate/PhD scientists working at the Centre.



These include more than 50 with PhD training, and cover a range of scientific disciplines including medicinal chemistry, biochemistry, molecular and cell biology, pharmacology, physiology and experimental psychology. Although the laboratories are organised into departments of Chemistry, Biochemistry, and Pharmacology, the working unit for most scientists is a "Project Team", each of which has a mixture of scientists working together to attain some particular goals. There are a number of such Project Teams at any one time, ranging in size from more than 30 scientists to as few as three or four in exploratory projects. Our job is to translate some of the recent advances in knowledge in basic neuroscience research into potential new products that can be developed for the treatment of mental or neurological illnesses. We cover only the initial stages of drug discovery (synthesis and testing of a new chemical, assessing validity of new hypotheses) and recommend new drug candidates to the parent company for further development and ultimately clinical testing - a process which may take a further 7-10 years. Graduate and PhD scientists are responsible for planning and carrying out all of our laboratory research. They are supported by a large team of staff running special facilities, eg computer, information, animal, publishing resources, administration. Both graduates and PhD scientists have well defined career paths, with opportunities for promotion dependent both on scientific success and increased managerial responsibilities.

Among our major areas of current research interest are the excitatory amino acids (particularly NMDA receptor antagonists), GABA<sub>A</sub> receptor pharmacology, dopaminergic and 5-HT pharmacology, and the neuropeptides. In the latter field we have a longstanding interest in substance P and related tachykinins, and we have also been involved in developing novel non-peptide antagonists of cholecystinin receptors - a field pioneered by Merck. We also have an interest in the molecular pathology underlying Alzheimer's disease, and are undertaking some exploratory work on neurotrophic factors, as important areas for the future. Much of our work is published in the scientific literature and our company has a liberal attitude towards such publications and encourages scientists to attend

meetings at home and overseas. Indeed the Merck culture is almost a "publish or perish" one - particularly when it comes to scientific promotions!

Among the different sections of the laboratory, two which may be of particular interest to Members of The Physiological Society are the neurophysiology laboratory and the molecular neurobiology groups. These groups often work closely together on functional studies on expressed cloned receptors and an example of this is illustrated by our recent project on GABA<sub>A</sub> receptor subtypes. GABA<sub>A</sub> receptors contain a benzodiazepine recognition site which mediates the anxiolytic, anticonvulsant and hypnotic actions of the clinically used benzodiazepines. Evidence had existed for some time that there were subtypes of the benzodiazepine "receptor" (described as BZ<sub>1</sub> and BZ<sub>2</sub> and the cloning of the various subunits classes which comprise GABA<sub>A</sub> receptors provided a molecular basis for this. Functional GABA<sub>A</sub> receptors which contain a benzodiazepine recognition site are comprised of a mixture of  $\alpha$ ,  $\beta$ , and  $\gamma$  subunits and there are six variants of the  $\alpha$  subunit ( $\alpha_1$ ,  $\alpha_2$ ,  $\alpha_3$ , etc) and three of both  $\beta$  and  $\gamma$ . Expression studies indicated that if the  $\alpha_1$  subunit was present, the recombinant receptor had a BZ<sub>1</sub> type pharmacology whereas the presence of  $\alpha_2$  or  $\alpha_3$  subunits conferred a BZ<sub>2</sub> type pharmacology. Further pharmacological variations are conferred by the  $\alpha_4$ ,  $\alpha_5$  and  $\alpha_6$  subunits. These results suggested the possibility of developing subtype-selective compounds which may have more selective effects *in vivo* than compounds which acted on all receptor types, eg it may be possible to develop compounds which were anxiolytic but not sedative and less likely to induce tolerance or dependence. The issue was how to tackle such a problem.

First of all we had to obtain all of the clones of the various receptor subtypes. Much of our initial exploratory work involved bovine clones and we discovered novel splicing variants of the  $\gamma_2$  subunits (Whiting *et al*, 1990). However, for drug discovery purposes we prefer to work with human receptors. This, in itself, was a major undertaking and involved the cloning from human brain cDNA libraries of all of the subunits corresponding to those described for other species. These then had to be inserted into an expression vector and transiently expressed in *Xenopus* oocytes and cell lines for functional and pharmacological studies. This allowed us to determine whether the various subunits would combine together to form functional receptors and to determine whether they resembled GABA<sub>A</sub> receptors that occur endogenously (Wafford *et al*, 1993). Assuming that each functional receptor contains at least one  $\alpha$ ,  $\beta$ ,  $\gamma$  subunit, there is a total of 54 possible receptor variants! Therefore, much of our initial work was to determine which subunit combinations actually exist *in vivo* in different brain regions in order to choose appropriate targets. This was achieved by a variety of different approaches. *In situ* hybridisation studies, both published in the literature and performed in our own laboratory, enabled us to determine where in the brain the mRNAs for the various subunits were expressed and this allowed us to rule out some possible combinations and guess at other likely ones. Antibodies specific for individual subunits were raised and these were used to immunoprecipitate endogenous receptors that occur in brain (McKernan *et al*, 1991). The pharmacological properties of these receptors were then examined using radioligand binding studies which provided some insights into their likely subunit composition. The immunoprecipitated receptors could also be further probed on Western blots with antibodies specific for other subunits which gave direct evidence as to which subunits



went together within the same receptor complex. Using these approaches the number of likely subunit compositions of interest was reduced dramatically from the original 54 and to a more manageable number. Although these receptors were initially studied using transient transfections, this is a relatively labour intensive method and, therefore, a major step forward was the production of stable cell lines expressing GABA<sub>A</sub> receptors of predetermined subunit composition (Hadingham *et al*, 1992). As the constitutive expression of ligand gated ion channels in eukaryotic cell lines affects viability, vector containing the mouse mammary tumour virus promoter was used so that expression of the receptor was only induced following treatment of the cells with dexamethasone. The level of receptor expression induced in this way is very high and these cells are excellent for both radioligand binding and electrophysiological studies of recombinant human receptor pharmacology (Home *et al*, 1992, Home *et al*, 1993).

Now we have reached this stage the "easy" part has been done. What remains is to use the cell lines containing the recombinant human receptors to screen compounds which possess the appropriate selectivity profile and develop them as novel therapeutic agents!

The ability to use human receptors and other proteins expressed in stable mammalian cells represents a major advance, and a big change in the way that companies are able to undertake drug discovery research. It permits the use of the human target receptor/protein at the earliest stages of test screening. This does not, of course, eliminate the need to test compounds at some stage in whole animal models, but it does reduce the need for such experiments and avoids the possible pitfalls of species differences often encountered between animal and human systems.

Like other pharmaceutical company laboratories, we keep close contacts with academic research laboratories in Britain and overseas. Although Merck & Co is the world's largest pharmaceutical company, we are a relatively small part of the whole. We are able to offer only a limited amount of financial support to academic research laboratories in Britain. This is spent in a number of different ways: through small grants to support particular pieces of work, part-sponsorship of scientific meetings, funding named lectureships for overseas speakers at British universities and part-sponsorship of a total of 18 PhD students through the SERC CASE award scheme and the corresponding MRC scheme. Such students spend some part of

their PhD training working in the laboratories here, and are jointly supervised by an industrial and an academic supervisor. In addition, we enthusiastically support the training of sandwich students from various British universities who spend a year working in our laboratories as part of their undergraduate training. This is one of the best ways for a young scientist to find out whether a career in an industrial research laboratory is what they want. We believe it teaches another important lesson also - namely that good science can take place in an industrial setting.

We are often asked by academic colleagues what working in industry is like. The challenge of drug discovery is an exciting and difficult one, and often frustrating because of the unexpected pitfalls which line the way, but it can also be very rewarding. Perhaps the biggest difference in the way in which we do research is the emphasis we place on teamwork. The problems that need to be solved identifying new drug candidates cannot be solved by any one individual - it requires a team with many different sorts of expertise. There is a place in industrial laboratories for the gifted individual who wants to pursue a scientific idea, but it helps if you enjoy working with others.

*John Kemp and Leslie Iversen*

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of article number

## Careers for research scientists

I am grateful for the opportunity to write about this subject for the *Magazine* since The Physiological Society has always been a great supporter of ARMS (Association of Researchers in Medicine and Science); moreover this seems to be a very appropriate time to review progress.

### The changing climate

While ARMS, since its inception in 1978, has been concerned about all aspects of scientific research, it has in recent years concentrated its attention on the need for a career structure for researchers, especially in the biomedical sciences where so many are employed on short term contracts. During our long

campaign we have observed a major change in the climate of opinion. Thus in the early 1980s the scientific establishment (ie the Research Councils, the CVCP, government departments and the universities) largely dismissed our complaints as either unfounded or merely the moanings of a group of failed scientists. Now it is universally agreed that there is a serious problem which must be solved if research activity in the UK is to flourish, even at the current level of financial provision.

### Proposals from ARMS

We have always tried to put forward positive proposals and so, after lengthy discussions, Dr Steve Hopkins of the University of Manchester redrafted our discussion document *Careers in Research*. Copies are available from ARMS. In summary, emphasis is placed upon the need for increased responsibility to



be placed upon academic research institutions to manage their research resource, including personnel, efficiently and responsibly. This would entail extending their contractual obligations for managing research projects and the establishment of career grade research posts. It is suggested that, following an adequate monitored (and accredited) training and a probationary period, those researchers proving suitable would enter one of two career tracks, either for innovative and creative team leaders or for highly skilled support scientists.

### *The Royal Society*

The Royal Society in their report *The Future of the Science Base* made proposals which in some respects closely accorded with those of ARMS. They proposed for those who had demonstrated their aptitude for research an extension of their Research Fellowship programme, so that those who had secured support would be able to seek out institutions in which they could most fruitfully pursue their research. They also recognised the need for supporting the highly skilled scientists who do not become team leaders, although it is unfortunately entirely unclear whether they would be prepared to support them: it seems doubtful, so who would?

While ARMS welcomed these proposals, it is our view that the flexibility of movement calls for a national scheme of accreditation. We have noted that the Royal Society have not pursued this line in their evidence for the White Paper on Science and Technology due to be published in May-June.

As the Royal Society points out, mechanisms will need to be introduced to help individuals transfer to a different employment sector if they do not continue in a research career. It recommends that employers should seek to identify such persons at an early stage, give training for skills and capabilities other than purely scientific, and encourage an understanding both inside and outside academia of the value and nature of skills that have been acquired during postdoctoral research. ARMS very much supports these suggestions.

### *The White Paper*

With respect to the forthcoming White Paper we noted that at a recent press conference on 19 March the Minister, William Waldegrave, agreed that the matter of careers was very important but that it was too complex for resolution at this stage. More than 800 organisations and individuals submitted evidence for the White Paper. Many of the 250 documents selected for display in the House of Commons library, including the evidence submitted by The Physiological Society, (see the *Magazine* No 7, page 9), mention their concerns about the absence of a career structure.

### *The MRC's View*

The view of the MRC is that it already has a unified career structure in its Institutes and Units not only for the best research scientists but also for research support staff. The MRC claims, therefore that it has well-proven models that can be extended to help rebuild HEIs' career structures for research. The MRC states that "There is a strong case for a profession-wide system of accreditation to facilitate readier movement of scientists between employment sectors and thus minimise the loss to the profession when contracts come to an end." They further write that "the study by the Council of Science and Technology Institutes, commissioned by the Department for Employment, into the employment pattern of UK scientists, should be a valuable first step towards this goal."

### *The Wellcome Trust*

There are, too, welcome moves among the charities. Thus the Arthritis and Rheumatism Council now provides fellowships for five years which may be considered for three-year renewals. The Wellcome Trust, which in October 1992 was supporting some 630 Research Assistants at the 1A level, 195 at the 1B level, and 195 other fellowships, has just published a draft document for discussion entitled *The Career Development of Biomedical Researchers* which addresses many of the problems. The Trust suggests that it funds a series of renewable fellowships both for research fellows and for technical staff in departments receiving major Trust funding. In respect of the latter they point out that, according to the Advisory Council On Science and Technology (ACOST), support for technical staff in universities has decreased by 13% in real terms over the period 1980-1990. The Trust propose, therefore, that departments which have considerable Trust support should be able to apply for a grant for a technologist initially appointed for four years but renewable. Such support would not be tied to a particular research grant.

Concerning academics, the Trust suggest that the core of their support should be a Research Fellowship awarded for four years initially, reviewed at the end of the third year, and renewable for a total period of 16 years. There could then be promotion to an Advanced Research Fellowship, normally applied for by the age of 43. There are also Re-entry Fellowship Awards to cope with individuals (such as women with families) who have taken time off. Other competitive Fellowships and a few Wellcome Research Professorships would exist. These proposals certainly go some way towards producing better career prospects for those lucky enough to be supported by the Trust.

In addition to producing its discussion document, The Wellcome Trust has written to the ten leading research universities listing details of those whom it is supporting. They seek a discussion of the future management and support of all those over the age of 35. This should put the institutions on their mettle. ARMS welcomes this for it is our view that the universities are at present failing in their responsibilities as employers of large groups of contract researchers. At the risk of increasing bureaucracy, the universities should take into consideration the career prospects of its employees.

### *A way forward*

While ARMS welcomes the initiatives now coming from the charities and the Research Councils, our aim is still the achievement of some kind of national accreditation by the age of 30, and has given much consideration to this possibility. It is interesting, as already mentioned, that the MRC is in favour of such a scheme. One obvious development would be for the universities to collaborate in the launch of a new degree between that of PhD and DSc. Government support for such a move would not only assist the development of a career structure but would signal that the UK recognises the importance of scientists and appreciates that they need recognition as much as do accountants and lawyers. In the absence of a greater sense of responsibility on the part of employers and some national accreditation, I fear that the enlightened policy of The Wellcome Trust, while important, will not meet our national requirements or attract our talented youth to a career in scientific research.

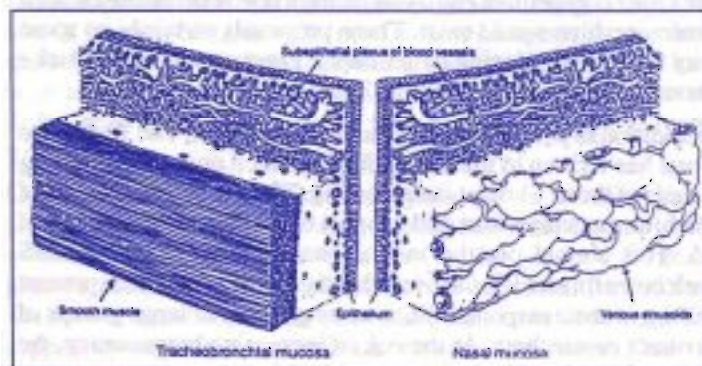
*Peter N Campbell*  
Chairman of ARMS



## Physiology of the airway mucosa and its relevance to asthma

Asthma is a disease of airway mucosal inflammation, with secondary smooth muscle contraction. A key role in the inflammatory process has been ascribed to the mucosal vasculature. Hyperaemia, interstitial oedema and exudate into the airway lumen are characteristics of the condition.

The airway mucosa has a dense subepithelial capillary network (Fig 1), probably related to the high metabolic rate of the epithelial tissue; both ciliary beating and active transport of ions and macromolecules are high energy-consuming processes. In asthma this capillary network is hypertrophic and the capillaries develop fenestrations, not seen in healthy airways. The postcapillary venules can be affected by inflammatory mediators such as histamine and bradykinin, and transudation of plasma, water and other constituents such as albumin takes place, extending into the airway lumen as exudate. In asthma the airway epithelium is damaged or even destroyed, making its protective barrier defective.

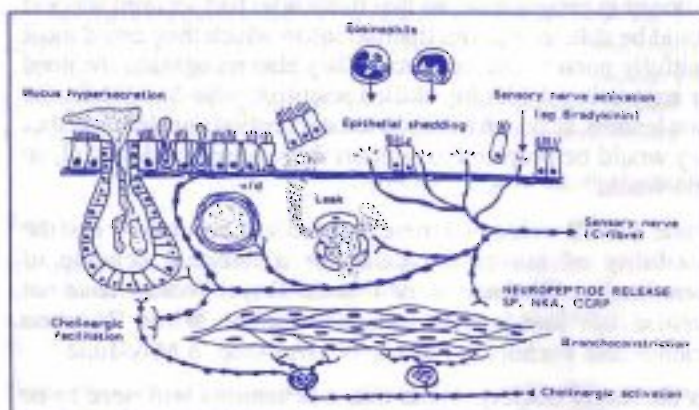


**Fig 1** This drawing emphasises differences and similarities between nasal and tracheobronchial vascular beds. A major obstructive mechanism of the nasal passages is filling of venous sinusoids (sinuses), which are less developed in the lower airways; here obstruction can be caused by tracheobronchial smooth muscle contraction. The epithelium and the subepithelial plexus of microvessels in nose and lower airways are actively involved in a plasma exudation process, both in normal mucosal defence and in inflammatory airway diseases such as asthma and rhinitis. From C G A Persson, in Butler (1992).

Deeper in the mucosa are capacitance vessels or sinuses. These are especially conspicuous in the nose, where they can distend and thicken the mucosa, improving air conditioning and filtration and, in the extreme, block the nasal cavity. They are also present but less developed in the tracheobronchial tree of many species including man. Direct measurements in sheep and dog show that when the mucosal vasculature is congested there can be considerable thickening of the mucosa, another feature of asthma. The physiological function of the capacitance system in the lower airways is unclear; unlike for the nose, a role in filtration and air conditioning seems unimportant.

Many inflammatory mediators are powerful airway vasodilators; these include histamine, bradykinin, 5-hydroxytryptamine and many prostaglandins. These either act locally by relaxing the

vascular smooth muscle or indirectly by release of endothelium-derived relaxing factor from the vascular endothelium. Other powerful dilator agents are the group of sensory neuropeptides including substance P, neurokinin A and calcitonin gene-related peptide. These neurotransmitters are released from sensory nerves by axon reflexes when the nerves are stimulated by irritants or inflammatory mediators, including those derived from mast cells in allergic reactions. A wide pattern of so-called neurogenic inflammation is seen, similar to the triple response in the skin. There is hyperaemia, oedema, gland secretion, epithelial dysfunction and possibly smooth muscle contraction (Fig 2). These are all features of the asthmatic condition.



**Fig 2** Possible neurogenic inflammation in the asthmatic airway via retrograde release of peptides from sensory nerves via an axon reflex. Substance P (SP) causes vasodilatation, plasma exudation and mucus secretion, whereas neurokinin A (NKA) causes bronchoconstriction and enhanced cholinergic reflexes, and calcitonin gene-related peptide (CGRP) causes vasodilatation. From Barnes, Chung & Page (1988).

Activation of the same sensory nerves will elicit not only axon reflexes but also central nervous reflexes via afferent fibres in the vagus nerves. These reflexes include airway smooth muscle contraction and submucosal gland secretion, and vasodilatation mediated both by a decrease in sympathetic vasoconstrictor tone and an increase in parasympathetic vasodilator tone. Thus the net effect of the local actions of mediators, of axon reflexes and of central nervous reflexes is to cause mucosal vasodilatation and thickening, and possibly oedema and exudate.

A similar condition may occur in patients, induced by exercise, hyperventilation or inhalation of cold air, common triggers of an attack of asthma. Unlike for the nose, where the vascular beds subserve important air conditioning and filtering functions, in the lower airways these mechanisms are poorly developed. However, cold air and the increased osmolarity of airway surface liquid associated with evaporation of water from the trachea can cause vasodilatation and presumably thickening of the mucosa, at least in some experimental animals and probably in susceptible human subjects. Again unlike for the nose, the tracheobronchial tree seems to have few or no arteriovenous anastomoses, and in this respect must be rather inefficient as an organ which can control heat and water loss.

The recent extensive studies on the physiology and pharmacology of the airway mucosa and vasculature have increased our understanding of the role they may play in conditions such as asthma. They also point to therapeutic possibilities, since it is relatively easy to inhale aerosols of drugs that act on the mucosa



and vascular bed. This is done for the nose with vasoconstrictor agents that can effectively treat some forms of rhinitis. For asthma most inhaled drugs are designed to act on airway smooth muscle or to inhibit inflammation. The use of agents targeted to affect the mucosal tissues such as blood vessels, glands and epithelium might provide an important therapeutic adjunct.

**John Widdicombe**

*Summary of a lecture delivered at the Society's symposium for final year undergraduates (Leeds, December 1992).*

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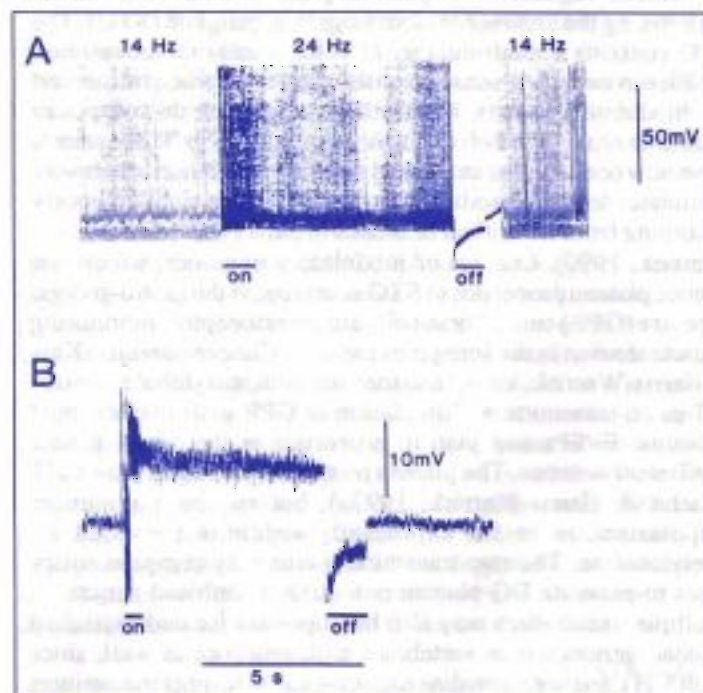
## Transmitter modulation and possible function of plateau properties in mammalian motoneurons

In the early 1950s Eccles and collaborators introduced intracellular recordings from mammalian spinal motoneurons. They concluded that these cells possess a simple set of ionic conductances and that local synaptic events spread passively along dendrites to the soma where a more or less linear summation of postsynaptic potentials ultimately may lead to action potential generation. This description thus attributed mainly passive response properties to motoneurons and suggested that motor activity is shaped and timed by neuronal connectivity at pre-motoneuronal levels. It is now known that vertebrate motoneurons possess a large number of different ionic conductances that contribute to the electro-responsiveness of motoneurons. Additionally, recent research has demonstrated that motoneurons possess complex transmitter-regulated membrane properties, such as plateau potential capabilities and bursting properties, which permit motoneuron spike activity to be dynamically shaped. Taken together, this implies that motoneurons can now no longer be considered as passive output elements in the spinal cord.

### Plateau potentials in mammalian motoneurons

Plateau potentials are intrinsic properties of neurons and are expressed as a prolonged maintained depolarised state. Transient depolarisations, eg a short barrage of EPSPs, can initiate a plateau potential which may remain for a long period of time before it either terminates spontaneously or is actively turned off by a brief inhibition. The plateau potential therefore allows the cell to possess two quasi-stable states of activity: one around rest and another at a more depolarised level. This property of two levels of excitability is referred to as a *bistable behaviour*. Schwandt & Crill (1977, 1980; see also 1984) first demonstrated plateau potentials in mammalian spinal motoneurons. In their preparation, the barbiturate-anaesthetised cat, plateau potentials were not easily seen unless motoneurons were exposed to a substantial pharmacological treatment (see later). In a series of experiments from our laboratory on decerebrated unanaesthetised cats, we have shown that plateau potential capabilities are spontaneously present in this preparation (Hounsgaard *et al* 1984, 1988a; Conway *et al* 1988; see Kiehn 1991a, b for reviews). The bistable behaviour in a motoneuron from one of these cats is illustrated in Fig 1. The motoneuron was shifted between two stable firing states by short-lasting synaptic excitation and inhibition (Fig 1a). The underlying plateau is

seen in Fig 1b, where the spike-generating mechanism has been inactivated. A bistable firing behaviour can also be initiated and terminated by short-lasting depolarising and hyperpolarising current pulses injected into the motoneurons.



**Fig 1** Bistable firing behaviour and plateau potentials in motoneurons. Intracellular recordings from spinal motoneurons in decerebrated cats. *a*. Brief synaptic excitation ("on"; see Hounsgaard *et al* (1988a) for further details) and inhibition ("off") shift the motoneuron between two stable states of firing frequency. *b*. In a different cell the spike initiating mechanism was inactivated by excessive prolonged depolarisation. Brief synaptic excitation and inhibition now initiates and terminates a prolonged depolarising plateau. Modified from Hounsgaard *et al* (1988a)

It is clear that the bistable behaviour allows motoneurons to fire action potentials, without a continuous synaptic drive, and that it endows motoneurons with a substantial computational power. The concept of vertebrate spinal motoneurons as purely passive followers must therefore be discarded.

### Motoneuron plateau potentials are transmitter controlled

The ability to generate plateau potentials in motoneurons is a conditional property. The bistable behaviour in decerebrated cats is dependent on activity in serotonergic and noradrenergic fibres (Hounsgaard *et al* 1988a; Conway *et al* 1988) descending



from nuclei in the brain stem. Motoneurons located below an acute spinal transection are not able to generate plateau potentials unless high doses of serotonergic (5-HTP: 5-hydroxytryptophan) or noradrenergic (L-DOPA: L-DOPA: L-b-3, 4-dihydroxyphenylalanine) precursors were given intravenously. Studies in an *in vitro* preparation of the turtle spinal cord (Hounsgaard & Kiehn, 1985, 1989; Hounsgaard *et al.* 1988b) confirmed these findings and showed that bath-applied serotonin (5-HT) induced plateau properties in motoneurons. In the decerebrate cat, at least, the descending serotonergic systems seem to be tonically active, allowing motoneurons to display bistable activity. The influence of monoaminergic fibres on motoneuron properties can be described as a permissive effect; that is, unpatterned activity in serotonergic or noradrenergic fibres uncovers the plateau capability that allows short inputs to trigger maintained motor output.

This situation is very similar to the ones known from studies of transmitter regulation of plateau properties in other motor systems, eg the crustacean stomatogastric ganglion (STG). The STG contains a small number of cells, mostly motoneurons, which can express plateau potential properties when influenced by modulatory inputs from other ganglia or the periphery (Hartline *et al.* 1988; Selverston & Moulins, 1987). These effects have now been studied extensively and it is possible to selectively stimulate identified modulatory neurons, while simultaneously recording from individual neurons in the STG (Katz & Harris-Warrick, 1990). One set of modulatory neurons, which can induce plateau properties in STG neurons, is the gastro-pyloric receptor (GPR) cells. These cells are proprioceptors monitoring muscle tension in the foregut of the crab, *Cancer borealis* (Katz & Harris-Warrick, 1989), and they use both acetylcholine and 5-HT as co-transmitters. Stimulation of GPR cells evokes rapid nicotinic EPSPs and plateau properties in the dorsal gastric (DG) motoneuron. The plateau properties are induced by 5-HT (Kiehn & Harris-Warrick, 1992a), but require a minimum depolarisation to be expressed, which is provided by acetylcholine. The two transmitters thus play complementary roles to generate DG plateau potentials. Combined actions of multiple transmitters may also be important for understanding plateau generation in vertebrate motoneurons as well, since both 5-HT and noradrenaline each co-exist with other transmitters in the descending spinal tracts (Jacobs & Azmitia, 1992). Unfortunately, there is no relevant data on this point available for the vertebrate spinal motoneurons. However, the picture which emerges from the studies above is that the plateau potential capability is a modifiable feature, which presumably can be turned on and off under different behavioural conditions.

The generality of the findings is stressed by recent studies in insects where plateau potentials have been reported in cockroach (Hancox and Pitman, 1991) and locust (Ramirez & Pearson, 1991) motoneurons. In the locust the expression of plateau potentials is octopamine dependent. Extracellular iontophoresis of NMDA can also induce bistable behaviour *in vivo* in spinal motoneurons in the cat (Engberg *et al.* 1984) and it is expected that future experiments will reveal other transmitter candidates.

#### The ionic mechanism for generation and induction of plateau potentials

The ionic mechanism for plateau potentials has been studied in a variety of different cells from both vertebrates and invertebrates (Llinas 1988; Hartline *et al.* 1988). In these systems the generation

of plateau potential arises from activation of slowly and/or non-inactivating  $\text{Na}^+$  conductances,  $\text{Ca}^{2+}$  conductances or some combination of these conductances. If the plateau is a conditional property, and not an endogenous one, induction of the plateau would be expected to require a change in the balance between outward and inward currents. In barbiturate-anaesthetised cats, bistable behaviour was seen after pharmacological reduction of outward currents and/or enhancement of inward currents (Schwindt & Crill, 1977, 1980, 1984).

Schwindt & Crill (1980) described a persistent inward current,  $I_p$ , as responsible for the plateau potential and suggested that  $I_p$  was mediated by  $\text{Ca}^{2+}$  ions. We have investigated the ionic basis for the serotonin-dependent bistable behaviour in the turtle spinal cord and found that the plateau itself is mediated at least in part by a non-inactivating L-like  $\text{Ca}^{2+}$  conductance (Hounsgaard & Kiehn 1985, 1989).

5-HT reduces the size of the slow afterhyperpolarisation, which is mediated by a  $\text{Ca}^{2+}$ -dependent  $\text{K}^+$  current. 5-HT seems therefore to induce a bistable behaviour by removal of an outward current, thereby uncovering the plateau current. It is, however, likely that 5-HT regulates other currents than the  $\text{Ca}^{2+}$ -dependent  $\text{K}^+$  current. Multiple effects of 5-HT are known from other systems (Nicol, 1988), and a recent study has indeed shown that 5-HT can release plateau properties in the DG motoneuron by enhancing a hyperpolarisation-activated inward current ( $I_h$ ) and decreasing an outward  $\text{Ca}^{2+}$ -dependent current (Kiehn & Harris-Warrick 1992b).

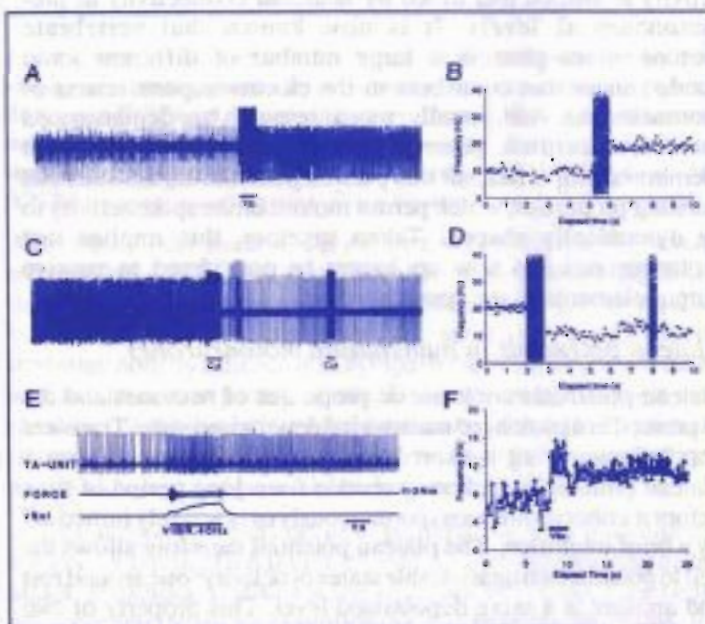


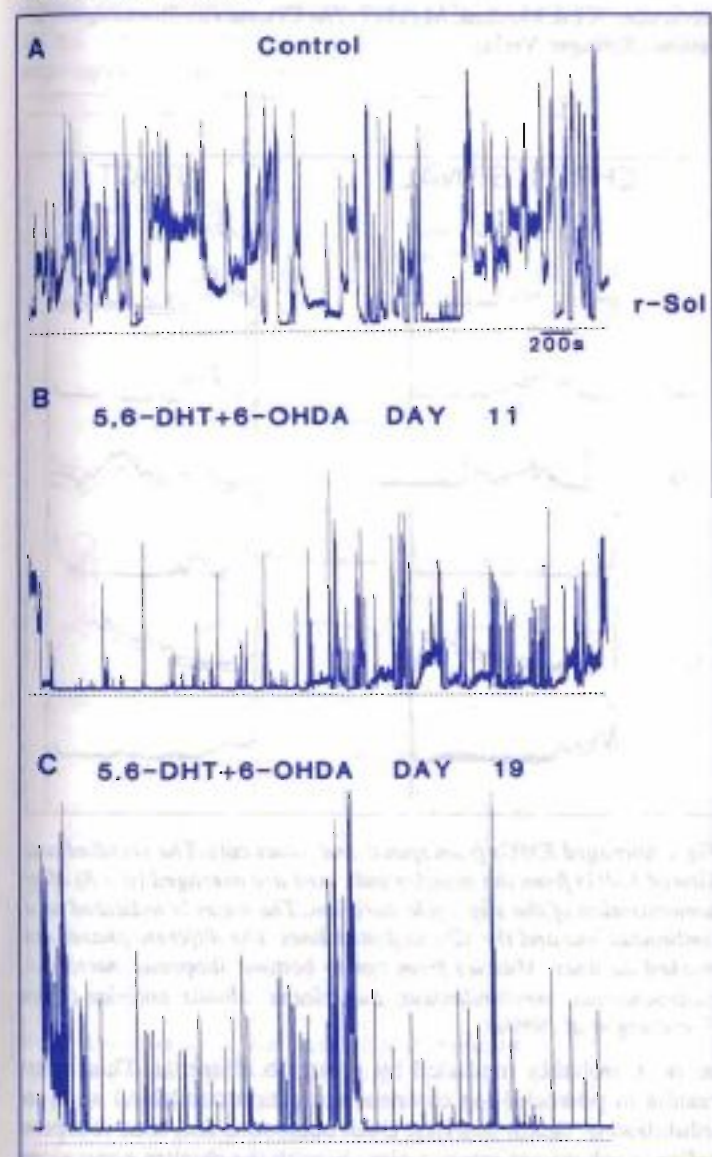
Fig 2 Bistable firing behaviour in soleus motor units in intact unrestrained rats (a-d) and in motor units in man (e-f). A brief stimulation of the tibial nerve (Tib, see Eken & Kiehn (1989) for further details) causes a maintained shift from a low frequency mode around 10 Hz to a high frequency mode around 20 Hz (actual frequencies vs. time in c). c-d. Maintained decrease in firing frequency in response to a short-lasting activation of skin afferents in the foot (Cut). The second stimulus was ineffective in changing the frequency further. e-f. Maintained frequency changes in single motor unit in tibialis anterior induced by short-lasting vibration ("VIBR") of homonymous muscle tendon. Lower traces in e display rectified and integrated gross-EMG. (a-d modified from Eken & Kiehn, 1989; e-f from Kiehn & Eken, 1992).



The main point to make here is that due to the slow inactivation of the plateau current, plateau potentials can generate prolonged motor output, which can last for minutes in the absence of synaptic drive.

### Consequences for motor behaviour

The fact that motoneurons possess plateau properties implies that under some circumstances they have an active role in shaping the final motor output. It is clear that plateau properties provide an important amplification mechanism: the response to brief synaptic inputs is enhanced both in intensity and duration. Furthermore, strong synaptic inputs will rapidly activate or deactivate the plateau, while weaker inputs will be ineffective or need longer duration.



**Fig 3** Monoamine-depletion-induced changes in soleus EMG pattern. The figure shows 1 hr recordings in the same rat at the same time during the day but at different times after giving 40 mg 5,6-dihydroxytryptamine (5,6-DHT) plus 40 mg 6-hydroxydopamine (6-OHDA) intrathecally. Note that the characteristic tonic EMG pattern seen in control animals (a) changes to a more bursty EMG pattern, with shorter periods of stable activity and longer periods of no activity after monoaminergic depletion of the lumbar spinal cord (the cord was depleted to less than 2% of control values at day 20). Data from Kiehn *et al* 1992.

The next step in the analysis is to address the functional role of plateau potentials in motor behaviour. The first question is whether a bistable firing pattern is present in intact animals. To answer this question we have used electromyographic studies of motoneuron activity in awake freely moving rats (Eken & Kiehn, 1989) and in man (Kiehn & Eken, 1992). Here bistable firing properties and sharp discontinuities in firing frequencies could be induced by reflex activation of the motoneuron pool and was also seen spontaneously during voluntary contraction (Fig 2). We suggest that activation of plateau potentials in motoneurons may account for this firing pattern, and that plateau potentials may provide a mechanism for maintaining continuous motor output without much tonic synaptic input, eg during posture. Interestingly, when descending monoaminergic fibres were destroyed selectively by neurotoxins (applied intrathecally at lumbar spinal level) the total tonic activity in the soleus muscle decreased markedly with a simultaneous increase in short-lasting, more burst-like events (Fig 3, Kiehn *et al* 1992). This pattern is apparently similar to the pattern seen in 8- to 15-day old rats (Eken *et al* 1990). The immature pattern is replaced by a more adult pattern at the age of 20 days. At this time the motoneurons receive an adult serotonergic innervation pattern and it is tempting to suggest a causal relation. To address this question further a longitudinal study of motoneuron membrane properties in the developing rat is required.

### Concluding remarks

In this review I have described the phenomenology, transmitter regulation and ionic basis for plateau potentials in mammalian motoneurons. It is clear from this work that motoneurons need to be considered as actively involved in the shaping and timing of normal motor behaviour. I have concentrated on a possible function for plateau potentials in supporting continuous motor output, eg in the upright position. Other aspects have been left out, eg the contribution of NMDA-induced bistability for motor output during rhythmic movements (see Grillner *et al* 1988) and the possible contribution of bistability to the development of cramps in man (Baldiessa *et al* 1991). Hopefully future studies will shed more light on the intrinsic electrical properties of motoneurons and their possible functional significance.

Ole Kiehn

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## Training of "spinal locomotion" in paraplegic patients: a promising approach?

During the last 15 years a rapid expansion in our knowledge of the neuronal basis of locomotion has been gained in quite diverse fields. The present report outlines how present knowledge in motor physiology has resulted and contributed to formulation of a potentially useful improved treatment of patients with motor disorders, specifically patients with spinal cord injury.

### Animal studies

There is general agreement that locomotor movements in mammals depend primarily on neuronal mechanisms within the spinal cord that can act in the absence of any afferent input (for review see Grillner & Dubuc, 1988). It has been known for several years that chronic spinal cats are able to perform stepping movements. After a lower thoracic spinal transection, administration of DOPA or noradrenergic agonists can elicit locomotor movements (Grillner 1969). If the hindlimbs are placed on a treadmill the movements adapt by and large to the treadmill speed. The hindlimb muscle activity is not as well modulated as in the intact animal, but nonetheless there is well-co-ordinated activity between the limbs and between antagonistic muscles (Fig 1: Forssberg *et al* 1980 a, b). Until recently it was thought that stepping movements could not occur in patients with transections of the spinal cord. This was based on the belief that supraspinal circuits, which of course would be lesioned in such patients, are more dominant in humans than spinal circuits in animals (cf Kuhn, 1950). Recently, an integrated drug and locomotor training approach has been described for subjects with partially damaged spinal cords. This combined the action of a noradrenergic agonist and a serotonergic antagonist coupled with gait training by treadmill stimulation (Fung *et al* 1988).

The spinal cord is capable of generating complex patterns of muscle activation in the legs following stimulation of cutaneous afferents (flexion reflexes) which are modulated by the central pattern generator. This effect has been well documented for example in the cat (Duysens, 1977). Furthermore, more recent animal experiments have demonstrated effects on the spinal pattern generator following load receptor stimulation in leg extensor muscles (Conway *et al* 1987). The latter afferent input

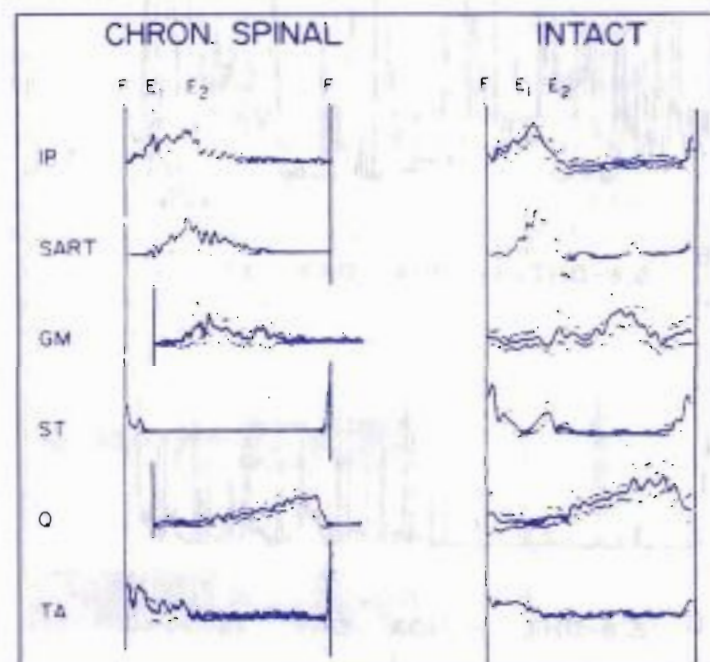


Fig 1 Averaged EMGs from spinal and intact cats. The rectified and filtered EMGs from the muscles indicated are averaged ( $n = 8$ ) after normalisation of the step cycle duration. The mean is indicated as a continuous line and the SDs as dotted lines. The different phases are marked as lines. Muscles from top to bottom: iliopsoas, sartorius, gastrocnemius, semitendinosus, quadriceps, tibialis anterior (from Forssberg *et al* 1980a).

is most probably mediated by group Ib afferents. This input results in powerful leg extensor activation combined with an inhibition of flexor activity. Both cutaneous and load receptor reflex mechanisms interact closely with the rhythm generators during fictive locomotion in the spinal cat (Conway *et al* 1987).

### Human studies

Our own contribution to this field has been extensive electrophysiological and biomechanical investigations concerning the physiological basis of human locomotion and pathological deviations in patients with supraspinal lesions (see Dietz, 1992, for review). Many investigations have been focused on the pathophysiological basis of spasticity in patients suffering spinal and supraspinal lesions (Dietz *et al* 1981; Berger *et al*



1988). In patients with spastic hemiparesis, the compensatory reaction following a perturbation of stance on the unaffected side consists of a biphasic pattern of hindlimb muscle activity. The first response can best be described as a polysynaptic spinal stretch reflex response. This response is absent on the spastic side, except for its later declining components. This remainder of the first response and the activation of the antagonistic muscle is identical on both the unaffected and the spastic side (Fig 2). The latter part of the pattern was assumed to be centrally programmed (at the spinal level) and triggered by the perturbation impulse (Berger *et al* 1988). The conclusion was that in these patients, locomotor programmes generated from within the spinal cord were still intact, although there was an impairment of spinal reflexes which normally adapt the EMG pattern to the actual environmental irregularities. The impairment of these spinal reflexes was attributed to the absence of the normal supraspinal influence on these reflexes.

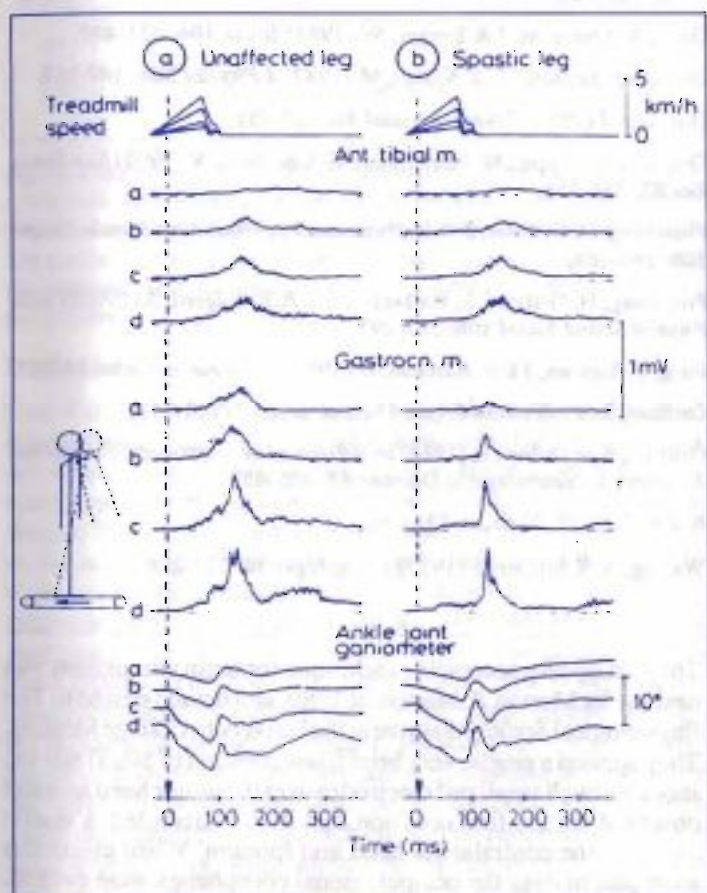


Fig 2 Mean values of the rectified and averaged ( $n=10$ ) leg muscle EMG responses together with the ankle joint movements (starting with an angle of about 90 deg on both sides) following backwards directed acceleration impulses during stance. Unaffected (a) and spastic (b) leg of 11 patients with spastic hemiparesis. a-d, different accelerations ( $5.5 \text{ ms}^{-2}$ (a);  $11.1 \text{ ms}^{-2}$ (b);  $16.6 \text{ ms}^{-2}$ (c);  $22 \text{ ms}^{-2}$ (d)). Impulse duration was constant. Arrows indicate onset of displacement (from Berger *et al* 1988).

Two further lines of evidence further support the proposal that humans, as well as other mammals, possess a pattern generator within the spinal cord that is capable of interacting with afferent input. First, the locomotor pattern in spastic subjects is similar to that in children at an age when the supraspinal control has not yet matured (Berger *et al* 1984a). Second is the short time delays for reflex transmission (Berger *et al* 1984b, Dietz *et al* 1987).

### Postural adjustments in water

Functional, complex, hindlimb muscle EMG patterns can be evoked in healthy subjects by stimulation of cutaneous afferents (Duysens *et al* 1990), or of load receptors within the leg extensor muscles (Dietz *et al* 1992). The existence of load receptors was suggested on the basis of observations made on postural adjustments during water immersion (see Fig 3: Dietz *et al*, 1990). Appropriate control of the gain of postural reflexes requires both muscle proprioceptive input and an additional peripheral input which should be "gravity" dependent. To investigate such receptors, the buoyancy of the body in a water-filled pool has been used to simulate the effect of weightlessness. During immersion there existed a close relationship between actual body weight and the magnitude of the EMG responses after both backward and forward displacement. Therefore, the function of proprioceptive reflexes in the stabilisation of posture depends on the presence of contact forces opposing gravity. Extensor load receptors were thought to signal changes in the projection of the body's centre of mass with respect to the feet. In addition, an influence of dopamine receptor antagonists on spinal reflex mechanisms was demonstrated during postural control in healthy subjects and patients (Dietz *et al* 1990).

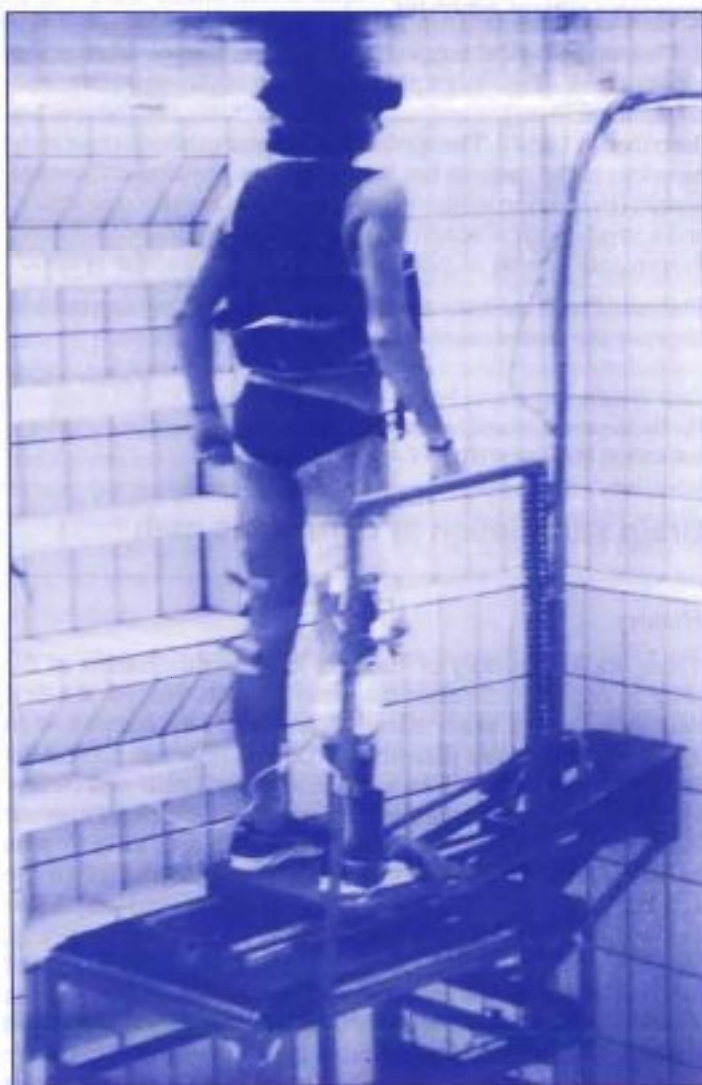


Fig 3 Subject standing under water on a pneumatically movable platform to induce backward and forward displacements. The subjects breathed through a snorkel. Buoyancy was partly compensated for using a lead vest with different loads. EMG activity from thigh and lower leg muscles were recorded together with joint movements.



Preliminary observations have shown that it is possible to induce stepping movements in paraplegic patients (incomplete lesions) and that the patients can profit from such training (Wernig & Muller, 1992). Training subsequently allowed patients to walk on a static surface for 100 to 200 m while voluntary activity remained absent in the paralysed limb when tested at rest.

### Potential applications

The aim of future research in this field is to investigate methods which allow controlled and functionally useful activation of spinal locomotor centres in paraplegic patients who are deprived of their supraspinal influence. These include:

1. Induction of stepping movements by treadmill stimulation, while the patient is partially supported. The aim is that the patient should learn to perform stepping movements on normal ground conditions. Long term follow-up is required to assess the effectiveness of locomotor training using the treadmill.

2. Facilitation of both the initiation and performance of stepping movements after induction of spinal reflex mechanisms (cutaneous- and extensor load-receptor) interacting with the locomotor pattern generator.

3. Pharmacological support for the performance of stepping movements (for example, noradrenergic agonists and serotonergic antagonists) in conjunction with the approaches described in 1 and 2. The application of these methods is not only harmless to the patients but they also have physiotherapeutical benefit (by moving joints in a natural way to prevent contracture) and a psychological benefit in that patients experience stepping movements as well as stimulating the cardiovascular system.

The use of such methods may represent a promising approach to improve the motor capabilities of paraplegic patients.

**Volker Dietz**

*Volker Dietz was recently elected to chair the department for paraplegic patients at the University of Zurich.*

## Brain stimulation in conscious man

### History

There is a long history of attempts to bypass the barrier of the skull in order to stimulate the brain beneath. Indeed, the first demonstration of brain stimulation in man by Bartholow in 1875, was made on a patient in whom an ulcer had eroded the skull so severely that a large portion of the brain was clearly visible around the central areas of cortex. Needles were inserted into the lateral part of the brain substance and used to pass electric current. The stimulus resulted in movements on the contralateral side of the body, just as demonstrated only a few years earlier by Ferrier and by Fritsch & Hitzig. Unfortunately, the intact normal skull proved more of a problem. Several workers in the 1950s attempted to stimulate the motor cortex using trains of electric stimuli lasting several seconds passed through large plate electrodes attached to the scalp. They were generally unsuccessful, mainly because of the severe discomfort produced by the large electric currents that were needed. It is said that one famous neurophysiologist even had old gramophone needles knocked into his skull in an attempt to get electric stimuli to the visual cortex, but failed.

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The first widely acceptable technique for brain stimulation was devised by Merton & Morton in 1980, and demonstrated to The Physiological Society that year at the University College Meeting. They applied a single, very brief (time constant of 50  $\mu$ s) electric shock through small pad electrodes over the motor hand area and observed, on the first occasion that it was attempted, a visible twitch in the contralateral hand and forearm. When electrodes were placed over the occiput, visual phosphenes were evoked. Unfortunately, the technique was still relatively uncomfortable, although much better tolerated than if trains of stimuli had been used. Since most of the applied stimulating current flows along the surface of the scalp, rather than into the brain, it causes local pain and a large contraction of the scalp muscles.

In 1985, the magnetic stimulator was introduced by Barker *et al.* In this technique, a large electrical capacitance is short-circuited through an insulated coil of 5-20 turns of copper wire held over the scalp. Large currents (typically 5000 A or more) flow transiently through the coil and produce an equally large and transient magnetic field (2 T) perpendicular to the coil. The field penetrates the brain readily, and, because it changes rapidly (decaying to half maximum in 50-100  $\mu$ s or so), it induces electrical eddy currents within the tissue. They flow maximally in an annulus under the coil, and circulate in the opposite direction to the capacitor discharge within the coil (see Fig 1). In a way, the magnetic field acts as a carrier of electric current



into the brain. With most present day stimulators, the currents in the brain have a similar time course as that produced with the electrical method. However, the technique is virtually painless since the currents induced on the scalp are little different from those induced in the brain. Because of this, the technique has achieved widespread acceptance.

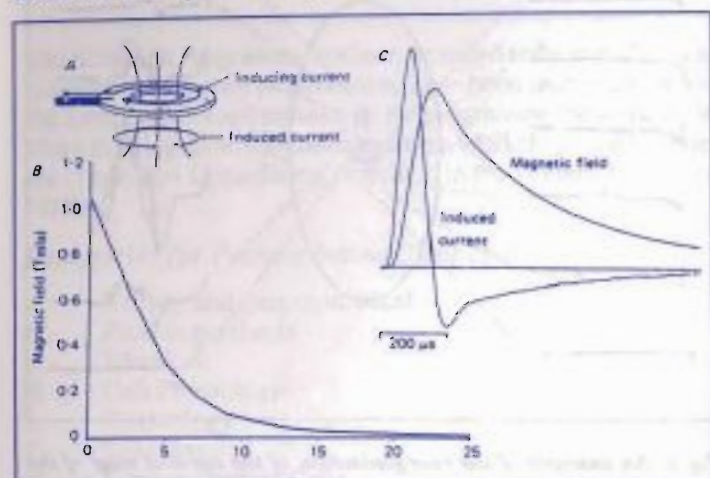


Fig 1 a, Diagram of a typical round magnetic coil showing the direction of the inducing and induced currents. b, Peak magnetic field strength related to the distance perpendicular from the flat surface of the coil. The device was operating at half maximal strength. c, Time course of the magnetic field and induced current. (From Hess et al 1986, with permission.)

### Limitations

One of the drawbacks to both electrical and magnetic forms of stimulation is that it is not possible to localise the stimulus very accurately. The surface of the brain is about 2cm below the scalp, and in man the central sulcus can extend another 2cm deeper. This means that even a very small focal electrode placed on the scalp will activate a large mass of tissue. With magnetic stimulation, the situation is, if anything, even worse. A focal magnetic stimulus implies using a small coil. However, the magnetic field from a small coil falls off with distance much more rapidly than that from a large coil. Thus, if we imagine stimulating a structure 3cm beneath the scalp, there is a trade-off between focality and strength of the stimulus. It is not readily possible to overcome this limitation by making an extremely powerful, but small stimulator. Large currents in a coil of wire cause the windings to repel each other. This repulsion causes the click which can be heard when a coil is discharged. Very large currents in a small coil cause the wires to repel each other with so much force that the windings physically break apart.

Some improvement in focality has been achieved by winding coils in the shape of a figure of eight, rather than a circle. The advantage of the "8" shape is that when the coil is wound so that the current flows in the opposite direction around each periphery of each loop. Thus the stimulating power is effectively concentrated along this bar. The limitations of strength and focality described above still apply so that, in practical terms, the size of the junction region of a figure of eight coil is limited to some 4-6cm by 1-2cm. Whether this is a reasonable estimate of the stimulated area within the brain is unknown.

A curious feature of magnetic stimulation is that it can activate different structures within the brain compared with conventional electrical stimulation. This can be seen very clearly when stimulating over the hand area of the motor cortex. If responses are recorded from contralateral hand muscles, then the latency

to electrical stimulation is 2ms or so shorter than if magnetic stimulation is used. Since there is good evidence that both forms of stimulation activate the same descending pathway (and both forms of stimulation give the same latency when used to activate peripheral nerve), the implication is that the mode of activation of the brain is different with the two methods. This unexpected result is thought to be a consequence of the pattern of current flow induced by the magnetic field. It turns out that, for rather complex physical reasons, the majority of the current induced by the magnetic field flows parallel to the surface of the brain (whether this is parallel to the skull, or follows the gyri and sulci of the brain, or some compromise between the two is not known). Unlike the situation with a focal electrical stimulus, there is a negligible amount of radial current flow. Presumably this difference in current flow leads to preferential activation of different structures by the two techniques. Which structures these are is an active source of controversy at the present time.

### Applications

The lack of knowledge of precisely what in the brain is being activated by magnetic brain stimulation, and where this is happening, obviously limits the use of the technique. However, despite these limitations a surprising amount of progress has been made. I should like to highlight three main areas of research in the field of motor control: clinical use in diagnosis and prognosis, investigation of motor reorganisation after injury, and investigation of connections between different parts of the brain and the motor cortex.

Clinically, the main use of magnetic brain stimulation is to measure the conduction time in the central motor pathways from brain to spinal cord. A selection of muscles in the arm and leg may be recorded and the latency of EMG responses measured after stimulation of the contralateral motor cortex. The conduction time in peripheral motor nerves from spinal cord to muscle is subtracted from this value to obtain the central motor conduction time (see Fig 2). This value is prolonged in many patients with diseases which affect the central motor pathways, such as multiple sclerosis or cervical spondylosis. It is an easy technique to use, but its yield, in terms of the proportion of subclinical abnormalities that are detected, is relatively low. In other words, clinical examination of the motor system is almost as likely to pick up abnormalities in the central motor tracts as magnetic stimulation.

Nevertheless, when clinical examination is difficult, measurements of central motor conduction can be invaluable. For example, surgical procedures on the spinal column carry a small risk of damage to the spinal cord itself, either through direct trauma, or by inadvertent interruption of the blood supply to one or two segments. It is now common to use somatosensory monitoring, in which a nerve in the leg is stimulated and the afferent volley tracked as it ascends the spinal cord by recording from epidural electrodes proximal and distal to the site of operation. However, there have been occasional reports in which somatosensory monitoring has proved normal throughout an operation, yet the patient has woken up paraplegic. The implication is that it is possible to produce separate damage to somatosensory and motor pathways. This can now be avoided by additional monitoring of conduction in descending motor pathways. A stimulus (usually electrical, since the apparatus is cheaper and the patient anaesthetised) is given over the motor area of scalp, and large motor volleys recorded by the epidural electrodes as they descend the cord. Any sudden decrease in size or increase in latency is a warning to the surgeon that damage may be occurring.



Examination of motor function in young infants is difficult. However, measurements of central motor conduction provide a possible objective method of defining motor abnormalities. Studies in normal children have shown that the central motor conduction time *decreases* rapidly in the first 2-3 years of life, reflecting the myelination of the pyramidal tract over that period (Fig 2). Comparisons of conduction in infants suspected of brain damage with those of normals may therefore allow early detection of corticospinal dysfunction. It is thought that the earlier appropriate physiotherapeutic treatment is begun, the more chance there is of influencing the development of the motor system. Studies have also begun at the other end of the age range, with attempts to relate corticospinal conduction time after a stroke to the eventual functional outcome, again with implications for the type of treatment that might be most appropriate in each case.

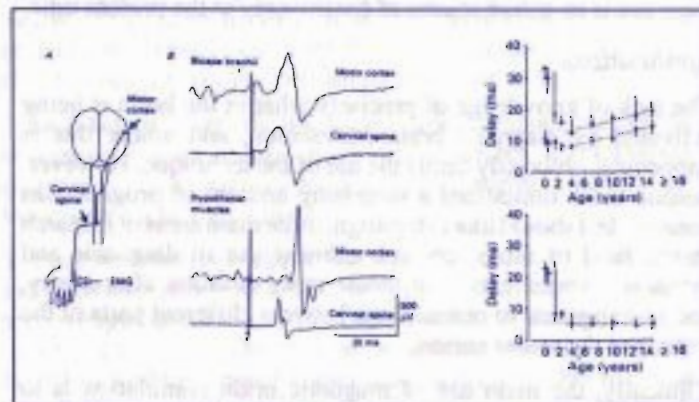


Fig 2 Left, diagram of the method of obtaining central motor conduction times with magnetic stimulation. Stimuli are given over the motor cortex and the spinal nerve roots over the cervical enlargement (to estimate peripheral conduction time). EMG responses can be recorded after stimulation at each site from biceps and hypothenar muscles. The lower pair of each traces is the response to cortical stimulation. Right, average latencies to hypothenar muscle activation in children of different ages after stimulation of the cortex and cervical enlargement (top graph). Note the very long central motor conduction time in children below 2 years, and the approximate constancy thereafter. (From Eyre et al 1991, with permission.)

It is now known that the central nervous system can undergo substantial reorganisation after injury to peripheral structures. For example, amputation of a digit in a monkey does not produce a "hole" in the cortical representation of the hand corresponding to the areas formerly devoted to that finger. Instead, adjacent parts of the hand representation enlarge and occupy that space. The same seems to happen in the motor system. Evidence in man which supports this comes from studies of the motor cortex representation in patients with amputation or after traumatic spinal cord injury. In these experiments, a small, relatively focal, magnetic coil is used to stimulate the scalp at 1 cm intervals, and the size of EMG responses evoked from each site is measured. In patients with amputation of a limb, or part of a limb, the representation of muscles immediately proximal to the level of the lesion is increased compared with controls (Fig 3). Since there is no evidence in these muscles to indicate any change in the organisation of their connections within the spinal cord, the implication is that there has been some form of reorganisation at a higher, probably cortical level. A similar phenomenon occurs even in normal subjects after temporary anaesthesia of a limb. Such results have been taken as supporting the hypothesis that the motor cortex map is extraordinarily labile, and that it is maintained by afferent input from the periphery.

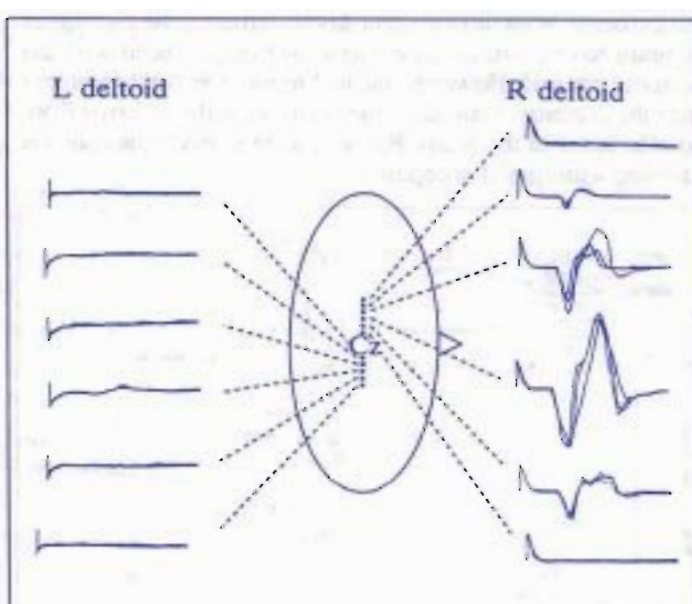


Fig 3 An example of the reorganisation of the cortical map of the deltoid muscle in an amputee with a four-year traumatic amputation of the right arm. The outline of the head shows a view from above indicating the position of the stimulation sites relative to the vertex (Cz). They are spaced at 1 cm intervals. The EMG responses on each side of the head are larger and can be obtained from more sites on the scalp contralateral to the amputation. A very small response is obtained only from one site contralateral to the normal arm. (From Cohen et al 1991, with permission.)

Finally, two stimulators can be used to investigate connections between different areas of the brain and the motor cortex. This has been demonstrated for probable pathways from the cerebellum to motor cortex, and from the contralateral to ipsilateral motor cortex. Thus stimulation over either the cerebellum or contralateral motor cortex (the conditioning stimulus) can, at an appropriate interval (5 ms for cerebellum, or 7 ms for contralateral cortex), reduce the size of EMG responses produced by stimulation of the ipsilateral motor cortex. The conditioning stimulus on its own has no effect on the excitability of spinal mechanisms at these intervals, so that the effect seems to be due to an inhibitory effect of cerebello-cortical and cortico-cortical pathways respectively. The effectiveness of these connections changes during movement and in disease. Thus, interhemispheric inhibition is reduced when subjects perform the same task with each hand compared with having one hand relaxed and the other active, consistent with a role in bimanual hand control. Pathological reduction in the effectiveness of interhemispheric inhibition is associated with the cortical spread of excitation in certain forms of epilepsy. Patients with generalised cortical myoclonus have muscle jerks which involve the whole body, and which appear to arise in a small area of motor cortex in one hemisphere and spread rapidly through cortico-cortical pathways to excite the opposite hemisphere. No interhemispheric inhibition can be observed in these individuals.

John Rothwell

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## Events Organised or Sponsored by the Society

### IUPS Congress, Glasgow 1993: Update on the scientific programme

The Scientific Programme has been arranged and some Abstracts, submitted for poster presentation, have been incorporated into the Symposia or used to make up the programme for workshops. The following details of Poster sessions, Workshops and Lectures are in addition to the listing presented in the January Magazine, No 6.

#### Categories for Posters but no Symposia

- a Kidney and gastrointestinal
- b Protein synthesis
- c Blood
- d Cell Physiology
- e Toxicology
- f Teaching
- g Human Cardiac Cells

#### Workshops

- K Neurolab Preproposal Workshop
- L Human Cardiac Cells

#### Plenary Lectures

There will be four lectures. The topics will be:

Bert Sakmann: Molecular Components of Excitatory Neurotransmission in the Central Nervous System

Sidney Brenner: The Human Genome

Lewis Wolpert: Pattern Formation in Development

Terence Sejnowski: The Computational Brain

#### Named Lectures

The topics of the named lectures are as follows:

##### Fenn Lecture

Sir Bernard Katz: Neural Transmitter Release: From Quantal Secretion to Exocytosis and Beyond

##### Robert F Pitts Lecture

Walter Boron: Intracellular pH Regulation in the Renal Proximal Tubule

##### August Krogh Lecture

Axel Michelsen: Transfer of Information during Honey Bee Dances studied by means of a Mechanical Model

##### Society of General Physiologists Lecture

Ernest M Wright: Molecular Architecture of the Na<sup>+</sup> Co-transporter

##### The Adrian-Zotterman Lecture

Robert F Schmidt: Nociceptors in Deep Tissue: Afferent and Efferent Function in Health and Disease

##### Eric Neil Memorial Lecture

Bjorn Folkow: Integrative Physiology, its Increasing Importance in the Era of Molecular Biology - A Tribute to Eric Neil as Master of the Craft

#### Historical Lectures

John West	History of High Altitude Physiology
M Glickstein	History of Cerebellar Research
Pierre Dejours	Paul Bert
Sir Stanley Peart	History of Autonomic Physiology
Tilli Tansey	Sir Henry Dale

### Designated Sessions at the UCL Meeting

#### Muscle Contraction Special Interest Group

There will be a meeting of the Muscle Contraction Special Interest Group at the forthcoming meeting of the Physiological Society at University College London. Time has been set aside to discuss future plans for the Group and for the election of a new convenor.

Michael A Ferenczi

#### Sensorimotor Control Group

There will be a Designated Session of the Sensorimotor Control group at the UCL Meeting (30 June - 2 July). Three Posters will be presented on Thursday 1 July and there will be 14 Oral Communications given in the afternoon of Wednesday 30 June. Subjects include cat spinal interneurons, fusimotor neurones, models of inputs to cat inspiratory motoneurons, and several papers on normal and disturbed motor control in man. There are also papers on oculomotor physiology and vestibulo-ocular physiology.

There will be a short Business Meeting at the conclusion of this session. Our next Designated Session will probably be at the Bristol Meeting in February next year. I would like to invite a speaker for this Meeting. Suggestion please!

I am hoping to organise a Motor Control Party at the IUPS Meeting on the evening of Tuesday August 3: an informal gathering for those interested in all aspects of motor control. Try and come!

Roger Lemon

#### Somatosensory Physiology Special Interest Group

There will be a Designated Session of the Somatosensory Special Interest Group at the UCL Meeting of the Society. This Group has recently changed its name from "CNS: Somatosensory Mechanisms". Fourteen talks and Two posters have been arranged, suggesting a full and interesting session. It is also intended to elect a convenor for the next few years and to discuss broadening the scope of our activities. Anyone with an interest in this branch of physiology should ensure their name and address is added to our mailing list by contacting me at the Meeting or writing to me at the Dept of Physiology, University of Wales, Cardiff CF1 1SS.

Malcolm Roberts



## Leicester revisited

Though it is doubtless not for a member of the home team to make the judgement, the Scientific Meeting of The Physiological Society in Leicester seemed highly successful. Well over 400 people attended various parts of the meeting. Lecture Theatre 1 of the Medical Sciences Building, which holds some 250, was more than full throughout the four hour Teaching Symposium on Ion Channels, at which the speakers were Peter Ruppersberg (Heidelberg), Oliver Dolly (Imperial College), David Brown, David Colquhoun and Malcolm Hunter. A similar number attended Peter Ruppersberg's outstanding lecture ("Molecular aspects of voltage-dependent block of ion channel") for the Ion Channels Designated Session. Similarly good reports were received about lectures from Pascal Ferre ("Metabolic adaptations during suckling and weaning" - Placental and Perinatal) and from R Borchardt ("The use of cultured intestinal epithelial cells to study the vectorial transport of bile" - Epithelia and Membrane Transport). All these lectures helped set the scene for scientific sessions at which there was good discussion about the science, with little nit-picking. The national press from the *Guardian* to the *Sun* reported extensively on Communication 76 by D C Rees on the effects of Nicorette gum on arterial haemodynamics.

Two innovations were tried concerning Posters. One of these seemed successful, the other less so. The decision to allow half an hour for discussion of the various Poster sessions, with a single slide being shown to represent each abstract, was very hard to make work, and by and



large the audience voted with their feet. But the Poster session on the first evening of the meeting, after dinner, was better attended than the sessions held during the subsequent days. A nearby bar doubtless helped the Posters go down in a relaxed fashion.

The Meeting was also graced by a wonderfully clear exposition of the "Role of cytoplasmic calcium in photoreceptor light adaptation" by Hugh Matthews, 1993 Wellcome Prize Lecturer of the Society, and by a medal ceremony at which Bridget Ogilvie, Director of the Wellcome Trust, presented medals to all those who have given the Wellcome Prize Lecture.

**Peter Stansfield**



### *Presentation of Wellcome Prize Medals*

*Bridget Ogilvie, Director of the Wellcome Trust, presents the Wellcome Prize Lecturers (1986-92) with their medals at the Leicester Meeting, April 1993, following the delivery of the Wellcome Prize Lecture by Hugh Matthews. From top to bottom: Kevan Martin (1986); David Eisner (1988); Andy King (1990); Hugh Matthews (1992)*



## Designated Sessions at the Leicester Meeting

### Comparative Physiology

The Comparative Physiology Group was represented at the Leicester Meeting by a Poster session which reflected our usual broad range of interests. Comparative Physiologists from Leicester presented work on sodium balance in mangrove crabs, spatial resolution in prawns and insect mechanoreceptors while other contributors modelled muscle cross-bridges described caffeine-releasable  $\text{Ca}^{2+}$  stores in crustacean muscle, the electrophysiology of locust foregut, and pharmacology of the dogfish heart.

The Group has planned a joint meeting with Comparative and Invertebrate Neuroscience at Southampton in September 1993, with a designated lecture by Allen Selverston from San Diego. We hope to stage a Symposium at this Meeting on Control of Visceral Function with guests from Italy and France. All Members are welcome to attend, contribute and invite guests who can contribute on any aspect of Comparative Physiology and Neuroscience.

E W Taylor

### Epithelia and Membrane Transport Group

The Epithelia and Membrane Transport Group met at Leicester with the Designated Session spread over the Thursday and Friday. Seven Posters for the Group were displayed on the Thursday morning and, as an innovation, each author was allowed to present one salient slide and allowed two minutes to describe the message for their Poster during the Poster approval session on the Thursday afternoon. The short presentations were followed by lively discussion of the Posters with the subsequent normal approval procedure. Although there was some vociferous and well presented argument against these short presentations of the Poster material, overall those present felt that they would like to continue with this experiment at subsequent Meetings. Indeed, it was suggested that the audience gained more from studying one slide than the standard six; perhaps all Communications should be limited to two minutes! What was apparent was that the most successful short presentations did not try to cram too much information onto their one slide (eg two or three figures from their Poster) but instead chose the most easily comprehensible and most important results or put up a slide illustrating a model system around which the author could discuss their results.

There were a total of 13 Oral Communications in the Designated Session, including papers presented by colleagues from Denmark and Chile. The subject matter for the papers presented in the Designated Session illustrated the large range of interests of the Group, including experiments on single channels, membrane transport systems, intracellular pH and calcium measurements in membrane vesicles and single cells, and fluid and solute transport across epithelia *in vivo* and *in vitro*. Tissues under discussion ranged from red blood cells to kidney, lungs and intestine. Lively discussion followed each presentation. Richard Naftalin reminded us all that cattle are incapable of making hard faeces, whereas in contrast the rabbit, being a clever animal, is able to form both hard and soft faeces. He demonstrated the suction pressure which the rat colon can generate was impressive, in excess of 2000 cm  $\text{H}_2\text{O}$ .



Bridget Ogilvie receiving the bronze Society dog, presented to the Wellcome Trust by David Cotterrell on behalf of the Society, in token of its appreciation of the Trust's longstanding support of physiology, at the Leicester Meeting, April 1993

Professor Ron Borchardt from the University of Kansas gave an excellent lecture on the use of cultured intestinal Caco-2 epithelial cells in the study of vectorial transport of the intestine. His lecture focused on the transport of bile acids as an example of an absorptive transport system in the intestine which has been studied using these cells. The Group were appreciative of the sponsorship from Costar Corporation for Professor Borchardt's visit to the UK, enabling him to be present at the Meeting.

The Group held a short Business Meeting on the Thursday afternoon and decided on a provisional programme for the next Meetings at which to hold Designated Sessions. These would include King's College London in December 1993, Newcastle in November 1994 and Cork in September 1995. All these dates are provisional, subject to the Society finalising its programme.

#### King's College London, 15-17 December 1993

Dr Sergio Grinstein (Toronto) has accepted an invitation to deliver an invited lecture at this Meeting on the topic of proton transport during neutrophil activation. The Meeting will be open for free Communications and Poster Communications. The dates for submission of abstracts for this Meeting are 20 September to 1 October 1993.

#### Newcastle, 9-10 November 1994

This Meeting will be a Joint Meeting with the Membrane Group of the Biochemical Society and the Epithelial Transport Club. There will be a one-day symposium with the theme of "Membrane channels, carriers and transport proteins". The programme for this symposium is being drawn up jointly with the Biochemical Society, but any suggestions for possible speakers should be forwarded to me as soon as possible. In addition, there will be free Communications and Posters of the usual format.

Barry H Hirst



### *Ion Channel Designated Session*

Peter Stansfield has already made mention of the successful Teaching Symposium and Designated Lecture organised by the Ion Channel Special Interest Group. There were in addition 37 Oral Communications and 12 Poster Communications associated with the Ion Channel Designated Session. These were well attended and followed by stimulating discussions.

Next April (1994) there will be a joint two day meeting between the Ion Channel Special Interest Group and the British Biophysical Society during the two days following the Meeting of the Society at Liverpool. This is being arranged by David Ogden and Mark Sansom of the British Biophysical Society, and Alasdair Gibb and myself for The Physiological Society. This joint meeting will be on "Structure and Function of Ion Channels" and suggestions for speakers (overseas as well as UK) would be most welcome.

*Noel Davies*

### *Joint Meeting of the Placental and Perinatal Special Interest Group of The Physiological Society and the Reproduction and Growth Group of the Nutrition Society*

This Designated Session was attended by 60-70 delegates of which about 25% were members of the Nutrition Society.

The high point of the meeting was the plenary lecture by Pascal Ferre entitled "Metabolic adaptations during suckling and weaning". This talk covered the physiological, endocrine, biochemical and gene expression transitions which regulate changes in glucose homeostasis following birth. Of particular interest were control mechanisms which allow the utilisation of glycogen stores at birth and during suckling, operating before lipogenesis becomes important at weaning. The clarity of Pascal's presentation was emphasised by the fact that it made no difference if slides were in French or English!

Eighteen Oral Communications and three Posters were presented which covered a range of subjects including:

- 1 The influence of the maternal environment on foetal development and possible consequences for postnatal life.
- 2 Regulation of lipid glucose homeostasis.
- 3 Normal and pathophysiological development of respiratory control.

The discussion was lively and informed, with particular emphasis being placed on some technical points, which presenters found extremely taxing. By the end of this meeting everybody felt they had gained from the experience and clearly the combination of physiological with nutritional scientists was a success.

*M Symonds and Mark Hanson*

### *Smooth Muscle Special Interest Group*

A one day symposium of the Smooth Muscle Group was held on the final day of the Leicester Meeting of the Society. There were 13 oral presentations, 5 Posters and a business meeting. In the morning session the smooth muscles were varied: uterus, vas-deferens, anococcygeus and vascular; but there was interested discussion after most, especially as the theatre gradually filled up during the course of the morning. At this Meeting the presenters of the Posters had been asked if they would like to present their main result in two minutes using one slide. All participants agreed to do this and all should be commended on keeping to time and giving a clear presentation. It has to be said though that, apart from fellow authors, the audience was slim, with afternoon tea being a compelling attraction. Perhaps when word spreads about how improved discussion of Posters is, more members will stay in subsequent Meetings. The posters ranged in topic from myocardial reactive hyperaemia to a method of measuring voltage dependence of activation of whole-cell  $Ca^{2+}$  channel currents in myocytes. Alan Chipperfield took the opportunity to give background behind their poster presentation on  $Cl^{-}$  measurements in arterial smooth muscle, showing that even when interference from other ions is taken into account,  $Cl^{-}$  is still substantially above its equilibrium value.

The afternoon communication session was well attended and lively. Two communications in particular raised much discussion. Firstly, the presentation by Dunn *et al* on structural and functional properties of pressurised resistance arteries from normotensive and L-NAME treated Brattleboro rats. The authors reported work showing no change in structure with hypertension and questioned the role of increased pressure *per se* in producing alterations in vascular structure. Much interested questioning of the presenter followed. The next communication by Beech *et al* and given by Tom Bolton showed evidence for nucleotide-diphosphate-dependent  $K^{+}$  channels in portal vein smooth muscle. The  $K^{+}$  channels opened when diphosphates were present at the intracellular surface and ATP sensitivity was only apparent at the intracellular surface and ATP sensitivity was only apparent after GDP had acted. The authors suggest that in smooth muscle it is diphosphates which play a critical role not triphosphate in these  $K^{+}$  channels. Debate followed led by Arthur Weston, whose colleagues from Manchester had earlier made presentations on rubidium antagonism of relaxation produced by levromakalim, suggesting that its relaxant effects are not mediated solely by  $K^{+}$  channel opening. The last communication of the session (Bolton *et al*) dealt with evidence that nucleotide diphosphate-dependent  $K^{+}$  channels were the site of action of levromakalim.

The Business Meeting saw the election of new convenors of the Group. Lucilla Poston and Jeremy Ward both of UMDS were elected. I wish them all the best. The next meeting of the Group will be in December at the Kings Meeting (abstract deadlines 20 September - 1 October). If the proposed Meeting venues for 1994 are confirmed, then there will be a Smooth Muscle symposium and a Special Interest Group Designated Session in Liverpool in April 1994 - don't say you haven't been warned!

*Susan Wray*



## Sight, Sound & Soma

On Tuesday 4 May, directly after the May Day Bank Holiday, the 5th Bristol Young Physiologist Symposium was held in the School of Medical Sciences, organised and hosted by two postgraduate students in the Department of Physiology.

Registration began at 9.30 am and coffee was served at 9.45 am. Participants arrived and began to get to know one another whilst the organisers rushed around checking that the speakers were all OK: there was at least one dramatic late arrival! At 10.25 am a brief welcoming introduction was given by Jonathan Gale, one of the organisers, explaining the background of the symposium and thanking all those who had been involved in its organisation, especially Lesley Anson, his counterpart. He also thanked the sponsors of the symposium: The Physiological Society, the Brain Research Association and the Department of Physiology, University of Bristol. Finally, he suggested that during the discussion period older members of the audience should hold back, at least initially, to allow the younger members a chance to ask questions and express their ideas.

The symposium got underway with **Sound**, the auditory session. Corné Kros was first to address the audience, which averaged 80 and was composed of mainly "young" scientists. He proceeded to explain the process of mechanotransduction in mammalian hair cells. Progress was made throughout the auditory system and Kathleen Nicol presented the possibility that there may be some "light at the end of the tunnel" regarding the regeneration of mammalian hair cells after damage. Moving centrally, Manuel Malmierca described his computer study of structure in the inferior colliculus, and then David McAlpine concluded this session by reminding us of how we process binaural information and also presented the interesting finding that recordings from neurones involved in this processing suggested that they have the ability to remember! The auditory session was closed and an excellent buffet lunch encouraged further discussion.

The meeting reconvened with **Sight**, the visual session. Talks by Muriel Bouvier and Linda McLatchie revealed how glial cells regulate glutamate concentrations in the retina, and how the cGMP-activated conductance of rod photoreceptors could be blocked by L-cis-diltiazem, respectively. Finally in this session, Helen Jones demonstrated that the visual thalamus was more complicated than we thought, and that the dorsal lateral geniculate nucleus may take a more active role in processing than previously described.

Tea was taken and then **Soma**, the final session on somatosensory physiology, began. Talks by Antonio Lopez-Garcia and Victoria Chapman discussed their experiments on sensory transmission mechanisms at the level of the spinal cord, *in vitro* and *in vivo* respectively. The session ended with an immunohistochemical study of persistent hyperalgesia by Gary Smith, which showed the expression of early onset genes in the spinal cord. He showed that treatment with the non-competitive NMDA antagonist, MK801, could prevent development of the hyperalgesia in this study.

To end the day, Jack Scannell gave an illuminating talk about his daring attempt to study cortical connections in various mammalian brains. He described his objective optimisation analysis of data, collected from various journals, the outcome of which was a "useful" organisational map of the cat and the macaque cortex. Finally, he illustrated how the organisation of the sensory systems differed in these two animals, suggesting that these differences may relate to their individual evolutionary histories.

The symposium was brought to a close at 6.00 pm and thanks given to the speakers for the high standard of their presentations. At that point a vote of thanks was issued to the organisers for all their hard work. The choice of adjourning to the pub or strolling to the Bristol docks was given to all participants: the choice was theirs. The day culminated in 40 of the participants enjoying a marvellous meal at the Bistro Musette restaurant in Bristol, where Lesley Anson told us all that she hoped we had enjoyed ourselves because she certainly had!

The meeting was a great success. Everyone agreed that they had gained something from the symposium. The major aim of the day was certainly achieved: young scientists met, addressed and talked with their peers, and also with more established physiologists, in the relaxed atmosphere of the day. Once again thanks should be given to The Physiological Society, the Brain Research Association and the Department of Physiology, University of Bristol, for financially supporting this symposium. Indeed, enough funds were available so that travel expenses for both speakers and postgraduate students could be reimbursed. The 5th Bristol Young Physiologist symposium undoubtedly followed the high standard of previous years and the organisers would like to thank all those who helped to make it a success. We look forward to the 6th!

Jonathan Gale



Left to Right: Lesley Anson, Linda McLatchie, Jonathan Gale, Helen Jones, Muriel Bouvier, Jack Scannell, Corné Kros, David McAlpine, Gary Smith, Manuel Malmierca, Antonio Lopez-Garcia, Victoria Chapman, Kathleen Nicol



## Editor's Note

No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the Notice. Notices for the September (Southampton) edition should reach the Editor or the Administration Office by 16 July 1993.

## CONTRIBUTIONS FROM NEUROSCIENCE TO CLINICAL NEUROLOGY

28-31 July 1993  
London

A scientific symposium to honour the career of Professor Tom Sears, of whom the speakers (from thirteen countries) are all former colleagues or close associates. Topics will include nerve conduction, demyelination, pain, motor control, respiratory control, neuronal death, survival development, and regeneration. Attendance will be by invitation. Those interested should contact one of the organisers (Hugh Bostock, Peter Kirkwood and Tony Pullen) at the Sobell Dept of Neurophysiology, Institute of Neurology, Queen Square, London WC1N 3BG, tel (071) 387 3611. ★  
(See the Letters section)

## IUPS CONGRESS 1-6 AUGUST 1993

Further information and registration forms from: IUPS Congress Office, CEP Consultants Ltd, 26-28 Albany Street, EDINBURGH EH1 3QH, tel (031) 557 2478, fax (031) 557 5749.

Correspondence for the Organising Committee should be sent to: IUPS Congress Office, Room F43, Hicks Building, University of Sheffield, Hounsfield Road, Sheffield S3 7RH. Telephone calls to: (0742) 758688, fax (0742) 758688. ★★

## NATO Advanced Research Workshop NONLINEAR PHENOMENA IN EXCITABLE PHYSIOLOGICAL SYSTEMS 8-12 August 1993

Leeds University

Grants available for some UK mathematical biology postgraduates and recent postdocs. Further details from: Dr Arun V Holden, Dept of Physiology, University of Leeds, Leeds LS2 9JT. ★  
(See page 9 for further details)

## BASIC AND CLINICAL PERSPECTIVES IN VISION RESEARCH 9-10 August 1993

St Thomas' Hospital, London

A review symposium celebrating Professor Hisako Ikeda's contribution to this field. Further details from: Dr Huw Jenkins, Vision Research Unit, The Rayne Institute, St Thomas' Hospital, London SE1 7EH, tel (071) 928 9292 Ext 3407, fax (071) 928 0729. ★

## International Society of Arterial Chemoreception CHEMORECEPTORS AND CHEMOREFLEXES IN HEALTH AND DISEASE

9-13 August 1993

University College Dublin

Further information from: Dublin Chemoreceptor Meeting, c/o Prof R G O'Regan, Dept of Human Anatomy and Physiology, University College, Earlsfort Terrace, Dublin 2, Ireland. ★★

## European Society for Comparative Physiology and Biochemistry - International Conference HORMONES, BRAIN AND BEHAVIOR

24-27 August 1993

Tours, France

Further details from: Secretariat "International Conference on Hormones, Brain and Behavior", INRA - Reproductive Physiology - 37380, Nouzilly, France, tel (010 33) 47 42 79 18, fax (010 33) 47 42 77 43. ★

## European Placenta Group VTH MEETING

8-11 September 1993

Manchester

Further details from: Dr C P Sibley, EPG Secretary, Dept of Child Health, St Mary's Hospital, Hathersage Road, Manchester M13 0JH, tel (061) 276 6483/4, fax (061) 224 1013. ★

## The Bayliss and Starling Society ANNUAL MEETING

13-14 September 1993

Royal Postgraduate Medical School, London

International workshop on biological control systems: Genes, mRNA, regulatory peptides & growth factors. Molecular biology, physiology, pharmacology & clinical applications. Deadline for abstracts: 3 May 1993. Further details from: Kim Cyrus, Endocrinology Unit, 2nd floor, Francis Fraser Building, Royal Postgraduate Medical School, London W12 0NN, tel (081) 740 3242, fax (081) 740 3142. ★★

## European Working Group on Cardiac Cellular Electrophysiology

17th MEETING

17-19 September 1993

Graz, Austria

Further details from: Prof B Koidl, Karl-Franzens-Universität Graz, Institut für Medizinische Physik u. Biophysik, Harrachgasse 21, A-8010 Graz, Austria, or from: Dr H F Brown, University Laboratory of Physiology, Parks Road, Oxford OX3 7TN, tel (0865) 272454, fax (0865) 272469. ★★

## XIIth International Symposium on RESPIRATORY PSYCHOPHYSIOLOGY

20-22 September 1993

Wellcome Centre, London

Further information from: Miss Janette Shiel, Dept of Medicine, Charing Cross & Westminster Medical School, Fulham Palace Road, London W6 8RF, tel (081) 846 7176, fax (081) 846 7170. ★



**European Society for Comparative Physiology and Biochemistry - 15th Annual Conference  
BIOCHEMICAL AND PHYSIOLOGICAL EFFECTS OF  
POLLUTANTS AND TOXICOLOGICAL ASSESSMENT  
OF ENVIRONMENTAL QUALITY**

**20-23 September 1993**

**Genova, Italy**

Further details from: Piera Ponta, Consorzio Genova Ricerche, Via dell'Acciaio 139, 16152 Genova, Italy, tel (010 39) 10 6514000, fax (010 39) 10 6512981 ★

**Royal Society Discussion Meeting  
MOLECULAR BIOLOGY OF PRION DISEASES**

**22-23 September 1993**

**London**

Further details from: The Scientific Meetings Secretary, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG, tel (071) 839 5561, Ext 278, fax (071) 930 2170 ★

**European Neuroendocrine Association  
FROM BASIC SCIENCE TO CLINICAL  
APPLICATIONS**

**6-9 October 1993**

**and Postgraduate Workshops in Endocrinology  
NEUROPEPTIDES and PITUITARY TUMOURS**

**5-6 October 1993**

**Lisbon, Portugal**

Further details from: Prof G Fink, MRC Brain Metabolism Unit, 1 George Square, Edinburgh EH8 9JZ, tel (031) 650 3548, fax (031) 662 0240; or Prof L Sobrinho, Dept of Endocrinology, Portuguese Cancer Institute, 1093 Lisbon, Portugal, tel (010 35) 1 1726 9285, fax (010 35) 1 1726 1529 ★

**INTERNATIONAL SYMPOSIUM ON ANAESTHESIA**

**20-22 October 1993**

**Beijing, China**

Deadline for abstracts: 15 May 1993. Further information from: Mr Zhang Ming, PO Box 300, CICCST, Beijing 100086, China, tel (010 86 1) 8313335, fax (010 86 1) 8316091 ★★

**International Conference on  
GASTROINTESTINAL HORMONES AND  
GASTROINTESTINAL MOTILITY**

**25-28 October 1993**

**Beijing, China**

Deadline for abstracts: 15 July 1993. Further details from: Mr Ming Zhang, PO Box 300, CICCST, Beijing 100086, China, tel (010 86 1) 8313335, fax (010 86 1) 8316091 ★★

**International Symposium on  
QUALITY ASSURANCE PROGRAMMES IN  
HOSPITALS**

**1-3 November 1993**

**Beijing, China**

Further details from: Mr Zhang Ming, PO Box 300, CICCST, Beijing 100086, China, tel (010 86 1) 8313335, fax (010 86 1) 8316091 ★★

**2nd International Conference on  
SPORTS MEDICINE**

**2-5 November 1993**

**Beijing, China**

Deadline for abstracts: 3 July 1993. Further information from: Dr Jhang Ming, Beijing International Hotel, No 9 Jian Nei Dajie, Beijing, China, tel (010 86 1) 5126688 ext 1534, fax (010 86 1) 8316091 ★★

**9th Annual Symposium on Biotechnology  
THE NEW BIOLOGY OF CARBOHYDRATES**

**16-17 December 1993**

**UCL Medical School, London**

Sections on biosynthesis, biological activities, protein-carbohydrate interactions, crystallography of protein carbohydrate recognition. Further details from: Mrs B Cavilla, Institute of Biology, 20 Queensberry Place, London SW7 2DZ ★

**9th International Conference  
BIOCHEMISTRY OF EXERCISE**

**21-26 July 1994**

**Aberdeen**

Deadline for registration and submission of poster abstracts: 31 January 1994. Further details from: Dr R J Maughan, University Medical School, Foresterhill, Aberdeen AB9 2ZD, Scotland, tel (0224) 681818 Ext 52482, fax (0224) 662990 ★

**2ND WORLD CONGRESS OF BIOMECHANICS**

**10-15 July 1994**

**Vrije Universiteit of Amsterdam, The Netherlands**

Deadline for abstracts: 1 December 1993. Further information from: Biomechanics Section, Institute of Orthopaedics, University of Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands, tel (010 31 80) 613366, fax (010 31 80) 540555 ★★

**Wellcome Centre for Medical Science - one day  
Open Meetings**

The Wellcome Centre for Medical Science, in collaboration with the CIBA Foundation, is organising one day Open Meetings to follow a selection of CIBA Symposia. The calendar for 1993 is as follows:

- 23 July -** *Germline Development*  
**10 September -** *Biological Clocks and Their Adjustment: Molecular, Cellular and Neural Aspects*  
**29 October -** *Second-Stage Filtering in Vision*

The meetings will be held in the Auditorium of the Wellcome Trust Building at 183 Euston Road, London NW1 2BE. There is a registration fee of £20 (£10 concessionary rate for graduate students) for each meeting, which includes refreshments, lunch and documentation. Further information from: Jilly Steward (071) 611 8656 ★★



## Scientific Apparatus Recycling Scheme

The FEBS Council has agreed to support the above scheme which aims to assist the biochemists of Eastern Europe by recycling to them scientific apparatus that is at present surplus to the needs of those in the West. In 1993 a grant was received from the TEMPUS programme of the European Commission (EC) to support a visit to the UK by representatives of the biochemical societies of Hungary and Poland. They visited many laboratories and identified apparatus both small and large that would be useful for the biochemists in their countries. A further grant was obtained from TEMPUS to cover the cost of transport within Europe. The Biochemical Society has kindly made available some spare warehousing at Colchester on a temporary basis. This is being used to assemble and sort the apparatus prior to despatch in bulk to the biochemical societies of many countries in Eastern Europe who are responsible for the distribution within their countries. Items are only sent after their identification as being useful for the recipients. FEBS is paying all the costs involved in the transport of the apparatus to Colchester and usually for transport across Europe although assistance is sometimes provided by the recipient country.

SARS has been warmly welcomed by many laboratories in the UK and requests for apparatus are constantly being received from the East. It is clear that SARS will have to be a long term measure. Attempts are now being made to extend SARS to other potential donor countries. SARS is not limited to university departments and research institutes; for industry and publishers of books and journals are also helping. SARS is also co-operating with the Association of Clinical Biochemists with a view to helping biochemists in the clinics.

Large loads have been sent to Poland, Hungary, Romania and Lithuania. Other loads are being assembled for Latvia and the Czech Republic which will include Slovakia. A reconditioned electron microscope has also been sent to Romania. SARS has now been extended to books and journals. We have in mind that the most valuable are the last ten years of complete runs of good journals but there are requests for much longer runs.

SARS is also now extending to Africa thanks to a grant from The Nuffield Foundation which will enable apparatus to be sent to desperate laboratories.

As SARS Co-ordinator, I would be pleased to hear from anyone who has surplus apparatus, books or journals for disposal. I sometimes have a call for copies of the *Journal of Physiology* which I can send through the Ranfurly Library Service.

Prof Peter N Campbell, Biochemistry and Molecular Biology, University College London, Gower Street, London, WC1E 6BT, tel (071) 387 7050 ex 2169, fax (071) 380 7193 ★★

## Animal Research - Facing the Public

"I believe that it is extremely important that the scientists whose work requires them to use animals ... explain what they are doing and justify it to the public more openly and more actively than has been done in the past." Sir Walter Bodmer FRS, Director General, Imperial Cancer Research Fund.

The need to justify and explain animal experimentation may occur during conversations with friends, seminars with groups of students, or a formal lecture or debate before a wider public. It is easier to meet the challenge with convincing facts, telling examples and good statistics! People may also want to read more about the issues in their own time. All of us are aware of some of the arguments and of some of the available literature, but in fact there is a bewildering collection of materials from numerous sources designed for different age groups.

The Animal Welfare Sub-Committee of The Physiological Society has collected information from all over the world, dealing with the issues. It has been produced by scientists, health charities, and responsible organisations concerned primarily with animal welfare. The videos, posters, pamphlets and books will be on display at the stand *Animal Research - Facing the Public* in the Exhibition area at the IUPS Congress in Glasgow.

The Sub-Committee is anxious to learn from your experiences of dealing with these issues. The stand will be manned by *Members of The Physiological Society, who welcome your contributions and interest.*

## Animal Experimentation and the Future of Medical Research

Edited by Dr Jack Botting, Research Defence Society. Proceedings of a Meeting held by the Research Defence Society to examine, from a scientific and medical perspective, the future role of animal experiments in medical research without ignoring the ethical context and justification for that research. Eminent scientists and clinicians who spoke about their fields of work, consider the importance of animal experiments in each case, include: Richard Adrian, D K Peters, David Rees, Sydney Brenner, John Vane, David Hubel, Walter Bodmer. It runs to 96 pages and the current price is £16.95. Published by Portland Press. ★★

## Errata

The Editor extends his apologies to:

- Dr R J Pack, New Zealand, for misprinting his initials (page 2, issue No 7)
- Cambridge Research Systems, for the error in their dialling code (page 25, issue No 7): their correct telephone number is (0634) 720707



## William Harvey and the Circulation of the Blood

This film, made in 1978 by M de Burgh Daly, Douglas Fisher, Leonard Goodwin and Gweneth Whitteridge, gives a brief account of Harvey's education, and of the theories of the movement of the blood in the body before Harvey's time, before re-enacting Harvey's experiments, described in his *De Motu Cordis* (1628), that provided proof of his hypothesis of the circulation of the blood. This 16mm film costs £80 plus VAT plus postage.

Two versions are now also available on video (VHS): a 37 minute version (price £40.00 plus VAT plus postage) and a 27 minutes version (price £25.00 plus VAT plus postage).

Enquiries and orders should be made to: Dr Michael Clark, Audio Visual Resources Manager, the Wellcome Trust, 183 Euston Road, London NW1 2BE, tel (071) 611 8596/7 ★★

## Membership of The Physiological Society

Persons wishing to be considered for election to Membership of the Society at the 1994 elections are advised to ensure that their documentation reaches the Society's Administration Office by the end of August.

The minimum criteria for consideration by the Committee for inclusion on the Membership ballot (as Ordinary or Foreign Members) are:

- 1 A candidate must have given at least one Communication or Demonstration in person to the Society.
- 2 A candidate must have published at least one full research paper on a physiological subject in a reputable journal. This paper will form part of the documentation considered by the Committee, so that in the case of a paper that has more than one author details of the contribution made by the candidate must be provided.
- 3 The candidate must obtain the signatures of SIX Members of the Society who will sign a statement declaring that the candidate is well known to them, is practising in physiology or a cognate subject and is likely to remain so, fulfils the criteria for Membership and is likely to benefit from Membership of the Society and take part in its activities.

There are currently two classes of Membership for which individuals can be considered. Candidates for Ordinary Membership will reside in the British Isles or have worked for a substantial period in the British Isles or have served the Society in some significant way. Candidates for Foreign Membership will normally reside outside the British Isles.

Full details and forms are available from the Administrator (Membership), The Physiological Society, Administration and Publications Office, PO Box 506, Oxford OX1 3XE, tel (0865) 798498, fax (0865) 798092.

## Contributors

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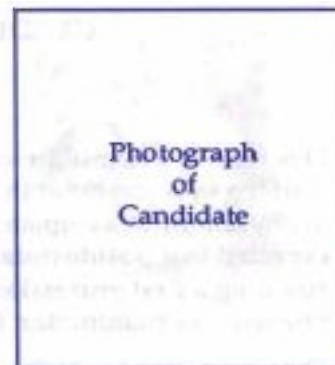


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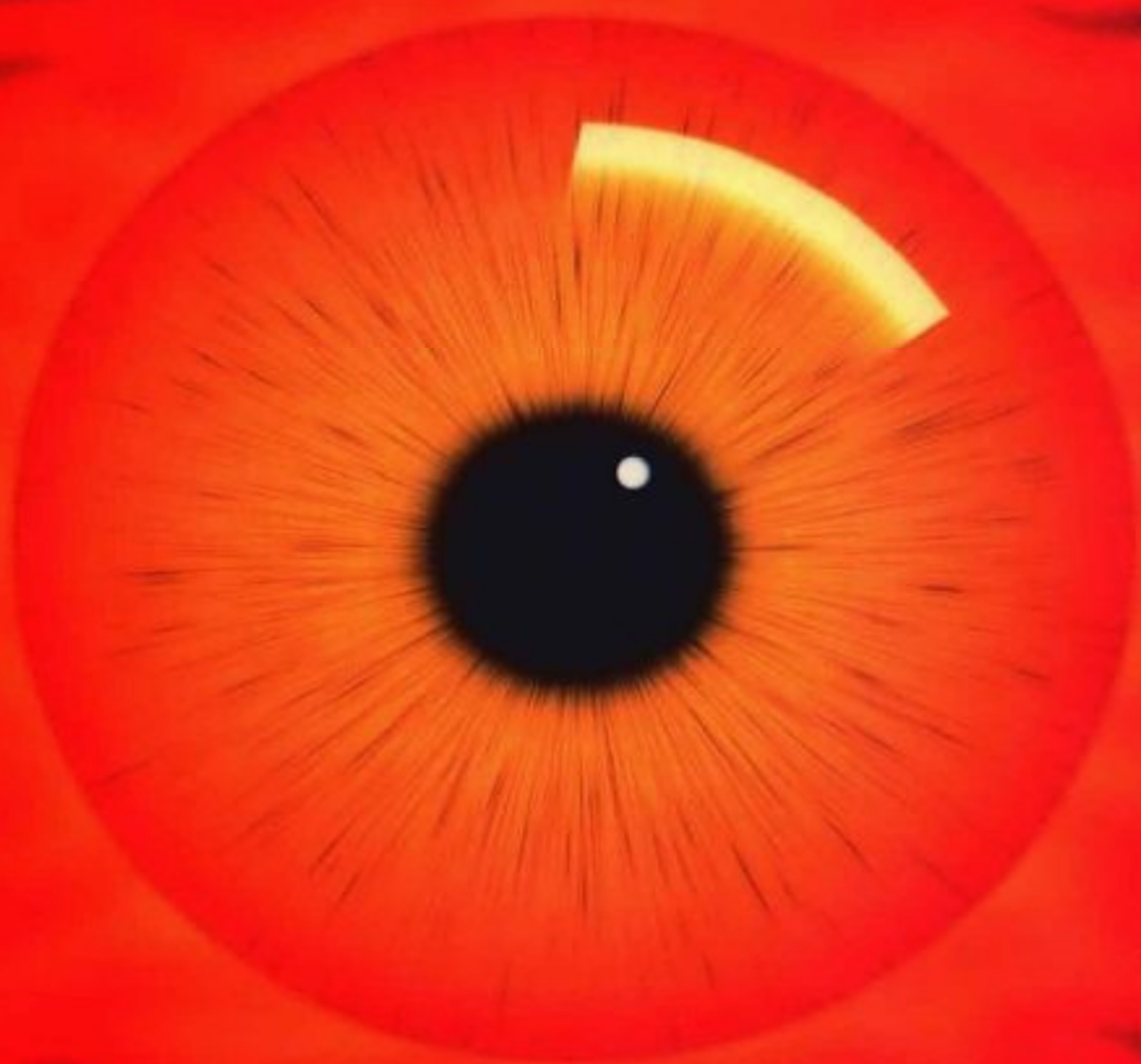
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